

[1]王月飞,廖凯,卢乐乐,等.乙肝病毒X蛋白通过激活c-myc诱导肝卵圆细胞的恶性转化[J].第三军医大学学报,2014,36(10):996-1001.

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乙肝病毒X蛋白通过激活c-myc诱导肝卵圆细胞的恶性转化:

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Title: Hepatitis B virus X protein induces malignant transformation of hepatic oval cells by activating c-myc gene

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摘要: 目的 研究c-myc对乙型肝炎病毒X蛋白(Hepatitis B virus X, HBx)诱导肝卵圆细胞恶性转化的影响。方法 通过HEK293细胞扩增腺病毒获得高滴度的Ad-EGFP和Ad-HBx,分别感染肝卵圆细胞株WB-F344细胞,通过RT-PCR和Western blot验证HBx蛋白对c-myc表达的影响。应用特异性对应c-myc基因的siRNA转染各组细胞。运用体外成瘤法、流式细胞术、细胞迁移实验,观察c-myc特异性siRNA对HBx诱导卵圆细胞恶性转化的影响。结果 与空白对照组Ad-EGFP相比,实验组转染Ad-HBx后,细胞中的c-myc表达水平增高;WB-F344-HBx细胞G₀/G₁期细胞比例显著降低、S期细胞比例显著升高;第1天3组细胞都以单细胞形式悬浮生长,随着时间延长,WB-F344-HBx细胞逐渐形成致密的细胞球体并且数量逐渐增多、体积逐渐增大;WB-F344-HBx细胞的迁移能力显著高于对照组。WB-F344-Mock和WB-F344-EGFP组之间各项指标均无明显差异。c-myc基因沉默后,3组细胞间各项指标均无明显差异。结论 乙型肝炎病毒X蛋白通过激活c-myc基因从而诱导肝卵圆细胞恶性转化。

Abstract: Objective To detect the effect of hepatitis B virus X (HBx) protein on hepatic oval cells and to investigate whether HBx protein can induce malignant transformation of hepatic oval cells after c-myc gene silencing. Methods The WB-F344 hepatic oval cells was separately infected with adenoviral vector (WB-F344-Mock group, blank control) and adenovirus expressing HBx protein (WB-

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F344-HBx group) or expressing EGFP (WB-F344-EGFP group, negative control). The expression of *c-myc* in the 3 groups of was confirmed by real-time PCR and Western blotting. The cell cycle, proliferation, ability of metastasis and tumorigenicity were detected with flow cytometry, metastasis experiment and tumor experiment *in vitro*, respectively. Results Compare with the WB-F344-Mock and WB-F344-EGFP groups, the WB-F344-HBx group highly expressed *c-myc* protein, showed significantly accelerated process of G₁/S cell cycle, and had stronger ability of metastasis and sphere formation. There was no significant difference in cell cycle, ability of metastasis and sphere formation between the WB-F344-EGFP and WB-F344-Mock groups. There was no significant difference in cell cycle, ability of metastasis and sphere formation between the WB-F344-HBx group and the WB-F344-Mock group as well as the WB-F344-EGFP group after *c-myc* silencing with siRNA. Conclusion HBx protein induces the malignant transformation of hepatic oval cells by activating *c-myc* gene.

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