

PAX-6在人乳腺癌中的表达及促进肿瘤转移的机制

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Title: Expression of PAX-6 in human breast cancer and its mechanism of promoting tumor metastasis

作者: 黄炜; 陈世满; 李雅琼; 李金友; 汪令成
湖北医药学院附属人民医院甲状腺乳腺血管外科, 湖北 十堰 442000

Author(s): Huang Wei; Chen Shiman; Li Yaqiong; Li Jinyou; Wang Lingcheng
Department of Thyroidectomy and Vascular Surgery, Renmin Hospital, Hubei University of Medicine, Hubei Shiyan 442000, China.

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摘要: 目的: 研究配对盒基因-6(paired box, Pax-6)在人乳腺癌组织中的表达和临床预后, 及PAX-6对乳腺癌细胞MB-231和MCF-7迁移和侵袭的影响及机制。方法: 以人正常乳腺上皮、乳腺癌及配对癌旁组织为研究对象; 通过实时定量PCR和免疫蛋白印迹实验分析PAX-6在乳腺癌组织、癌旁组织及正常上皮组织中的相对表达; 在线数据库分析PAX-6在乳腺癌中表达与预后的相关性; 免疫蛋白印迹实验分析PAX-6在乳腺癌细胞系中的相对表达, 选取高表达PAX-6基因的乳腺癌MB-231和MCF7细胞进行基因敲除, 设定敲除效率高的si-PAX-6(#1)为实验组($P < 0.05$), si-NC细胞为对照组; Transwell实验分析PAX-6敲除对细胞迁移和侵袭的影响; 实时定量PCR和免疫蛋白印迹实验验证PAX-6基因对细胞迁移和侵袭影响的机制。结果: 与正常乳腺上皮、配对癌旁组织相比, PAX-6在人乳腺癌组织中表达上调($P < 0.001$); 在线数据发现PAX-6的表达程度与乳腺癌的预后呈负相关, PAX-6基因表达程度越高, 患者预后越差($P = 0.038$); 与正常乳腺上皮细胞相比, PAX-6基因在乳腺癌细胞MB231、MCF-7和BT-549中高表达; 与对照组相比, 实验组si-PAX-6(#1)细胞迁移和侵袭明显受到抑制($P < 0.001$); si-PAX-6(#1)敲除后能下调Vimentin、N-cadherin、MMP2、MMP7和MMP9 mRNA和蛋白表达水平, 上调E-cadherin mRNA和蛋白表达水平。结论: PAX-6在乳腺癌的发生发展中起着重要的作用, 可能作为潜在的癌基因参与乳腺癌的进程。

Abstract: Objective: To investigate the expression and the clinical significance of PAX-6 in human breast cancer, and the effects of PAX-6 on migration and invasion of breast cancer cell lines MB-231 and MCF-7. Methods: qRT-PCR and Western blot were used to analyse the relative expression of PAX-6 in human normal breast tissues, breast cancer tumors and paired surgical margin tissues. PAX-6 expression and prognostic analyses were analysed through online database. Western blot was used to analyse the relative expression of PAX-6 in breast cancer cell lines. The si-NC was set as control group, and the si-PAX-6(#1) was the experimental group, to investigate the migration and invasion of malignant function of PAX-6 in breast cancer cell lines. We used transwell experiment to analyse the ability of cell migration and invasion. qRT-PCR and Western blot were used to analyse the basic mechanism. Results: PAX-6 expression were significantly up-regulated in breast cancer tissues compared to normal breast tissues and surgical margin tissues ($P < 0.001$), also prognostic analyses showed that higher levels of PAX-6 expression could have a worse survival rate ($P = 0.038$). And Western blot assay showed that PAX-6 were significantly up-regulated in breast cancer cell lines MB-231, MCF-7 and BT-549 compared with normal MCF-10A. Transwell assay showed that si-PAX-6(#1) in MB-231 and MCF-7 cell lines resulted in a significant decrease in migration and invasion cell than control group. Furthermore, the expressions of E-cadherin were significantly up-regulated, and the expressions of Vimentin, N-cadherin, MMP2, MMP7 and MMP9 were down-regulated in MB-231 and MCF7 cells. Conclusion: PAX-6 expression is up-regulated in human breast cancer, and appeared to be a functional oncogene regulating tumorigenesis of breast cancer.

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备注/Memo: -

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