中国肿瘤临床 2012, **Vol. 39** Issue (5): 249-253 DOI: doi:10.3969/j.issn.1000-8179.2012.05.003



# PXD101对人乳腺癌细胞MCF-7增殖及凋亡影响的机制探讨

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# The Effects of PXD101 on Proliferation and Apoptosis of Human Breast Cell Line MCF-7 and Its Mechanism

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摘要

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摘要 探讨组蛋白去乙酰化酶抑制剂PXD101对人乳腺癌细胞MCF-7增殖、细胞周期及凋亡的影响及分子机制研究。方法：应用不同浓度PXD101处理培养的乳腺癌细胞株MCF-7，通过赛唑蓝比色（MTT）法和平板克隆形成实验检测药物对细胞增殖的影响；Hoechst33342荧光染色法观察细胞形态变化；流式细胞仪PI染色法检测细胞周期变化以及Annexin V-FITC/PI双染法检测细胞凋亡情况；Westen blot检测p21、CyclinB1、PARP、Bcl-2以及Bax的蛋白表达。结果：PXD101以剂量时间依赖性抑制MCF-7细胞的增殖；荧光显微镜观察发现细胞核碎裂，出现凋亡小体；0、0.1、1、10 μmol/L PXD101作用24 h后，G2/M期细胞比例增加，分别为（12.66±1.55）%、（20.63±1.32）%、（23.20±1.82）%、（32.19±2.37）%（P<0.05），凋亡细胞也增加（P<0.05）；p21表达增多，CyclinB1表达减少，PARP剪切明显增加，Bcl-2表达减少，Bax表达增加。结论：PXD101在体外条件下能够明显抑制乳腺癌MCF-7细胞的增殖，诱导细胞周期阻滞及凋亡，并呈剂量依赖性。

关键词： 乳腺癌 PXD101 细胞周期 细胞凋亡

**Abstract**: This work aims to investigate the effect of PXD101, a novel potent histone deacetylase inhibitor, on the cell proliferation, cycle arrest and apoptosis of human breast cancer cell line MCF-7 and to preliminarily explore its molecular mechanism. Methods: MCF-7 cells were cultured in RPMI 1640 medium supplemented with 10% fetal bovin serum and were treated with PXD101 at varying concentrations. The methyl thiazolyl tetrazolium ( MTT ) assay and clonogenic assay were used to measure cell proliferation. Morphological changes of cells were observed by fluorescent microscope after staining by Hoechst33342. Flow cytometer was used to analyze the cell cycle arrest rates ( PI staining ) and the cell apoptotic rates ( AnnexinV-FITC/PI double- staining ). The protein expressions of p21, CyclinB1, PARP, Bcl-2 and Bax were detected by Western blot. Results: PXD101 was used to inhibit the proliferation of the MCF-7 cell line in a dose and time-dependent manner. Fluorescence microscope showed there were nuclear fragmentation and apoptosis bodies in the cells. Flow cytometric analysis indicated that PXD101 induced MCF-7 cells in G2/M phase were significantly increased. After MCF-7 cells exposed to different concentrations of PXD101, i.e., 0, 0.1,1 and 10μmol/L, for 24 h, the ratio of G2/M-phase cells was ( 12.66±1.55 ) %, (20.63±1.32 ) %, ( 23.20±1.82 ) % and ( 32.19±2.37 ) % respectively ( P < 0.05 ). The rates of apoptotic cells were also significantly increased, compared with the control group ( P < 0.05 ). PXD101 could up-regulate the protein expression of p21 and down-regulate the expression of CyclinB1. The cleavage of PARP and the expression of pro-apoptosis protein Bax were increased while the anti-apoptosis protein Bcl-2 was decreased. Conclusion: PXD101 in vitro can significantly inhibit the proliferation and can induce cell cycle arrest and apoptosis on human breast cancer MCF-7 cell line in a dose-dependent manner. PXD101 may become a new anti-tumor drug for human breast cancer.

**Key words**: Breast neoplasm PXD101 Cell cycle Apoptosis

收稿日期: 2011-07-13; 出版日期: 2012-03-15

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基金资助:

本文课题受国家自然科学基金（编号：81001186）和天津市应用基础及前沿技术研究计划项目（编号：10JCYBJC14100）资助

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引用本文:

. PXD101对人乳腺癌细胞MCF-7增殖及凋亡影响的机制探讨[J]. 中国肿瘤临床, 2012, 39(5): 249-253.

. The Effects of PXD101 on Proliferation and Apoptosis of Human Breast Cell Line MCF-7 and Its Mechanism[J]. Chinese Journal of Clinical Oncology, 2012, 39(5): 249-253.

链接本文:

http://118.145.16.228:8081/Jweb_zgzllc/CN/doi:10.3969/j.issn.1000-8179.2012.05.003　或　http://118.145.16.228:8081/Jweb_zgzllc/CN/Y2012/V39/I5/249

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