中国药理学与毒理学杂志 2005 19 (2): 98-102 ISSN: 1000-3002 CN: 11-1115/R

论著

三氟拉嗪诱发细胞凋亡及对DNA依赖蛋白激酶催化亚单位表达和P38磷酸化的抑制作用

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收稿日期 2004-7-3 修回日期 网络版发布日期 2008-6-13 接受日期 2004-11-29

摘要 目的 探讨三氟拉嗪（TFP）对肿瘤细胞生长的抑制作用和分子机制，寻找抑制肿瘤生长的作用靶分子。方法 用不同剂量TFP作用于人宫颈癌上皮细胞（HeLa），体外细胞计数绘制生长曲线；荧光染料染色及DNA琼脂糖凝胶电泳检测细胞凋亡；γ射线及TFP处理细胞观察TFP对细胞辐射敏感性的影响；Western印迹分析蛋白表达或磷酸化。结果 TFP作用后HeLa细胞的生长受到抑制，对γ射线的敏感性增加，且随着剂量的增加细胞凋亡的比率也增加。TFP还可有效诱导DNA修复蛋白DNA依赖蛋白激酶催化亚单位（DNA-PKcs）被切割，且可抑制辐射诱发的P38的磷酸化。结论 TFP可抑制肿瘤细胞的生长，对DNA-PKcs的表达和P38的磷酸化都有抑制作用。

关键词 磷脂酰肌醇3-激酶 催化域 三氟拉嗪 凋亡 辐射耐受性

分类号 R979.1

Effect of trifluoperazine on expression of DNA-dependent protein kinase catalytic subunits, phosphorylation of P38 and growth of HeLa cells

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Abstract

AIM To clarify the mechanism of trifluoperazine (TFP) inhibiting the growth of cancer cells and to find the target molecule of anticancer. **METHODS** HeLa cells were treated with different concentration of TFP and the growth of HeLa cells was measured *in vitro*. The method of fluorescent staining and DNA fragmentation electrophoresis in agarose gel was used to observe the characters of apoptosis. HeLa cells were treated with γ ray irradiation and TFP to detect the effect of TFP on cellular sensitivity. Western blot assay was used to test the expression or phosphorylation of protein. **RESULTS** TFP significantly inhibited the growth of HeLa cells, increased the radiosensitivity of HeLa cells. TFP also induced apoptosis in a concentration- and time-dependent manner. In addition, TFP could increase the degradation of DNA-dependent protein kinase catalytic subunits (DNA-PKcs) and inhibited the phosphorylation of P38 induced by ionizing radiation. **CONCLUSION** TFP can inhibit the growth of cancer cells. It also can suppress the expression of DNA-PKcs and the phosphorylation of P38.

Key words phosphatidylinositol-3-kinase catalytic domain trifluoperazine apoptosis radiation tolerance

DOI:

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