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丙酮酸乙酯通过下调蛋白激酶B通路抑制人胃癌细胞侵袭转移的研究

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Inhibitory Effects of Ethyl Pyruvate on Invasion and Metastasis of Human Gastric Cancer SGC-7901 Cells via Downregulation of Akt Pathway

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摘要

目的

探讨丙酮酸乙酯（EP）对人胃癌SGC-7901细胞侵袭转移的抑制效果及机制。方法噻唑蓝比色分析法 (MTT法)测定EP在胃癌SGC-7901细胞中的半数抑制浓度(IC50)。不同浓度EP加入到胃癌细胞后，实时定量PCR检测蛋白激酶B（Akt）的mRNA表达水平；Western blot检测Akt、p-Akt、基质金属蛋白酶-2 (MMP-2)和MMP-9的蛋白表达水平。划痕和Transwell实验评价胃癌细胞侵袭转移的能力。通过建立裸鼠皮下移植瘤模型，免疫组织化学进一步验证以上蛋白的表达水平。结果EP在胃癌SGC-7901细胞中的IC50为36.73 mmol/L。EP抑制Akt mRNA的表达及下调Akt、p-Akt、MMP-2和MMP-9的蛋白表达。划痕实验显示EP可抑制胃癌细胞的迁移运动能力；Transwell显示，与对照组（93.33±4.16）相比，EP 10 mmol/L组（75.34±4.73）、EP 20 mmol/L组（61.34±3.06）及EP 40 mmol/L组（39.00±3.00）的侵袭转移细胞数明显减少 (*P*均<0.001)。免疫组组织化学进一步证实了Western blot的检测结果。结论EP通过下调Akt通路抑制人胃癌细胞的侵袭和转移，对癌症具有一定的治疗效果。

关键词： 丙酮酸乙酯 蛋白激酶B 胃癌 转移

Abstract：

Objective

To explore the effects and molecular mechanisms of ethyl pyruvate (EP) on invasion and metastasis of human gastric cancer SGC-7901 cells.MethodsMTT assay was used to evaluate IC50 of EP on human gastric cancer SGC-7901 cell line.After different concentrations of EP (0,10 mmol/L,20 mmol/L and 40mmol/L) were added into SGC-7901 cells,the expression levels of protein kinase B (Akt) and phosphorylated Akt (p-Akt) mRNA were identified by real-time PCR,and the expression levels of Akt,p-Akt,matrix metalloproteinase-2 (MMP-2) and MMP-9 protein were detected by Western blot.The invasive and metastatic activities of gastric cancer cells were evaluated by wound-healing and Transwell assay.SGC-7901 xenograft tumor model was established,and the protein expression of Akt,p-Akt,MMP-2 and MMP-9 was further validated by immunohistochemical analysis.ResultsThe IC50 of EP on human

gastric cancer SGC-7901 cells was about 36.73mmol/L.EP administration inhibited Akt mRNA expression,and downregulated Akt,p-Akt,MMP-2 and MMP-9 protein expression.Wound-healing assay indicated that the migration and
exercise capability of SGC-7901 cells was reduced obviously;Transwell assay showed,in comparison with the control group (93.33±4.16),the number of invasive and metastatic cells infiltrated the matrigel in EP 10 mmol/L group(75.34±4.73),EP 20 mmol/L group (61.34±3.06) and EP 40 mmol/L group (39.00±3.00) was respectively decreased (each *P*<0.001).Immunohistochemical analysis further confirmed the expression levels of Akt,p-Akt,MMP-2
and MMP-9 protein shown by Western blot.ConclusionEP administration can inhibit the invasion and metastasis of

human gastric cancer SGC-7901 cells via downregulation of Akt pathway,and it may play a crucial role in cancer therapy.

Key words： Ethyl pyruvate　Protein kinase B　Gastric cancer　Metastasis

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