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论文

Gefitinib对激素非依赖性前列腺癌的治疗及其效应初探

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摘要：

目的 探讨受体酪氨酸激酶抑制剂Gefitinib在体内外对激素非依赖前列腺癌（HIPC）的抑制作用及其效应机制。方法 不同浓度的Gefitinib处理HIPC细胞株PC-3后24～120h，MTT法检测细胞生长抑制率，Western blot检测细胞表皮生长因子受体（EGFR）、蛋白激酶（Akt）、丝裂原活化蛋白激酶（MAPK）和蛋白激酶C（PKC）蛋白的表达水平。建立PC-3细胞裸鼠移植瘤，观察Gefitinib体内的肿瘤抑制率。结果 Gefitinib抑制PC-3细胞生长呈现时间-浓度依赖性，最佳抑制浓度为5ng/mL，最佳抑制时间为72?h，细胞生长抑制率稳定在50%～60%。与对照组比较，经Gefitinib处理后PC-3细胞中EGFR、Akt蛋白水平分别降低了70.44%和59.01%，而MAPK及PKC蛋白分别仅降低34.83%和33.40%。裸鼠实验结果表明，Gefitinib可显著抑制HIPC肿瘤的生长，抑制率高达53.95%，常规病理HE染色提示大片灶状癌细胞坏死。结论 Gefitinib可在体内外显著抑制HIPC的生长，其机制可能为通过降低癌细胞EGFR和胞内蛋白Akt的表达水平来发挥作用。

关键词： 激素非依赖性前列腺癌；吉非替尼；表皮生长因子受体；胞内效应蛋白

Inhibitory effect of Gefitinib on hormone independent prostate cancer in vitro and in vivo

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Abstract:

Objective To investigate the inhibitory effect of Gefitinib in the treatment of hormone independent prostate cancer (HIPC) in vitro and in vivo Methods The HIPC cell line PC-3 was treated with Gefitinib indifferent concentrations for 24-120?h, and then the cell inhibition ratio (CIR) was measured with MTT and expression levels of proteins, such as epidermal growth factor receptor (EGFR), protein kinase B (Akt), mitogen aetivatedprotein kinase (MAPK) and protein kinase C (PKC) were determined by Western blot. Results The inhibitoryeffect of Gefitinib on PC-3 cells′ growth showed a time and density-dependence, and the ideal inhibitory concentration and time were 5?ng/mL and 72?h, in which the CIR of PC-3 cells was 50%-60%. Compared with the control group, expression levels of protein EGFR and Akt were significantly decreased by 70.44% and 59.01% in PC-3 cells in the Gefitinib group; expression levels of MAPK and PKC was decreased by 34.83% and 33.40%. In an in vivo experiment, compared with the control group, the growth of HIPC tumors in the Gefitinib group was significantly inhibited by 53.95%.Conclusion Gefitinib could significantly induce inhibitory effects on growth of HIPC in vitro- and in vivo by down-regulation of expressions of EGFR and its intra-cellular effective proteins Akt in PC-3 cells.

Keywords: Hormone independence prostate cancer; Gefitinib; Epidermal growth factor receptor; Intra cellular effective protein

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