清肺化瘀解毒方对非小细胞肺癌细胞耐药的逆转作用研究Δ

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摘　要　目的　基于微RNA-641（miR-641）/胞外信号调节激酶（ERK）信号通路，探讨清肺化瘀解毒方（QFHYJDF）对非小细胞肺癌（NSCLC）细胞耐药的逆转作用。**方法**　以人NSCLC亲本细胞A549为对象，采用浓度梯度递增联合高浓度冲击策略构建吉非替尼耐药细胞系A549/GR。在筛选干预浓度及时间后，将耐药细胞分为对照血清组（20%空白血清作用48 h）、QFHYJDF含药血清组（20%QFHYJDF含药血清作用48 h）和常规培养组（常规培养48 h），检测各组细胞的相对活力和总凋亡率，以及细胞中miR-641和神经纤维蛋白1（NF1）、ERK1/2、磷酸化ERK1/2（p-ERK1/2）的表达水平。**结果**　与常规培养组和对照血清组比较，QFHYJDF含药血清组细胞的相对活力均显著降低，总凋亡率均显著升高，细胞中NF1蛋白的表达均显著上调，miR-641和p-ERK1、p-ERK2蛋白的表达均显著下调（$P<0.05$）。**结论**　QFHYJDF可抑制吉非替尼耐药肺癌细胞的增殖，促进其凋亡，上述作用可能与上调NF1蛋白表达、抑制miR-641表达及ERK信号通路活性有关。

关键词　清肺化瘀解毒方；非小细胞肺癌；吉非替尼耐药；miR-641/ERK信号通路

Study on the reversal effect of Qingfei huayu jiedu formula on drug resistance in non-small cell lung cancer cells

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ABSTRACT　OBJECTIVE To investigate the reversal effect of Qingfei huayu jiedu formula (QFHYJDF) on drug resistance in non-small cell lung cancer (NSCLC) cells based on the microRNA-641 (miR-641)/extracellular signal-regulated kinase (ERK) signaling pathway. **METHODS** The human parental NSCLC cell line A549 was used to establish gefitinib-resistant cells A549/GR by combining concentration gradient increment with high-concentration pulse strategy. After screening for optimal intervention concentration and duration, the resistant cells were divided into a control serum group (treated with 20% blank serum for 48 h), QFHYJDF-containing serum group (treated with 20% QFHYJDF-containing serum for 48 h), and the normally cultured group (normally cultured for 48 h). The cell relative viability, total apoptosis rate, as well as the expression levels of miR-641, neurofibromin 1 (NF1), ERK1/2, and phosphorylated ERK1/2 (p-ERK1/2), were assessed in each group. **RESULTS** Compared with the normally cultured group and the control serum group, the QFHYJDF-containing serum group exhibited significantly decreased cell relative viability and significantly increased total apoptosis rate ($P<0.05$). Moreover, the expression of NF1 protein was significantly up-regulated, while the expression levels of miR-641 and p-ERK1, p-ERK2 proteins were significantly down-regulated in the QFHYJDF-containing serum group ($P<0.05$). **CONCLUSIONS** QFHYJDF can inhibit proliferation and promote apoptosis of gefitinib-resistant lung cancer cells, which may be associated with up-regulating NF1 protein expression, down-regulating miR-641 expression, and inhibiting the activity of the ERK signaling pathway.

KEYWORDS　Qingfei huayu jiedu formula; non-small cell lung cancer; gefitinib resistance; miR-641/ERK signaling pathway

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