



## 自杀基因系统HSV-TK/GCV联合声动力疗法对人肺癌细胞NCI-446的体外杀伤实验

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### Effects of Treatment with Suicide Gene System HSV-TK/GCV Combined with Sonodynamic Therapy on Human Lung Cancer Cell NCI-446 in vitro

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#### 摘要

#### 目的

探讨自杀基因系统HSV-TK/GCV联合声动力疗法对人小细胞肺癌NCI-446细胞的体外杀伤作用。方法利用荧光和RT-PCR检测方法, 筛选出含HSV-TK基因阳性克隆株NCI-446/TK。用MTT法检测不同浓度的GCV对NCI-446/TK细胞的杀伤效应, 以及不同浓度混合NCI-446和NCI-446/TK细胞后的旁观者效应。同时, 将HSV-TK/GCV自杀基因系统与声动力疗法进行联合, 通过MTT法测定细胞存活率, 并以流式细胞术检测细胞周期及凋亡率。结果当GCV浓度为0.2 mg/L时, 筛选出的阳性克隆株NCI-446/TK细胞的生长受到明显的抑制 ( $P < 0.01$ ), 并且随着GCV浓度的递增, 抑制效应越明显。当NCI-446/TK细胞占总细胞的10%时, 有46%的混合培养细胞生长受到抑制 ( $P < 0.01$ ), 其抑制效应随NCI-446/TK细胞所占比例的增加而增加。将HSV-TK/GCV自杀基因系统与声动力疗法进行联合后, 其细胞存活率明显低于单一治疗组 ( $P < 0.01$ ), 并且G0/G1期细胞所占比例及凋亡率均高于单一治疗组。结论HSV-TK/GCV自杀基因系统的杀伤效应随着GCV浓度的递增而增强, 并且有明显的旁观者效应。与声动力疗法联合后, 其作用效果优于单一治疗组。

关键词: 自杀基因系统 声动力疗法 肺癌细胞 联合治疗

#### Abstract:

#### Objective

To observe the effects of suicide gene system HSV-TK/GCV combined with sonodynamic therapy on human lung cancer cell NCI-446 in vitro. Methods NCI-446/TK containing HSV-TK gene has been screened by the method of fluorescence and RT-PCR. MTT detected the damage effects of cells after NCI-446/TK treated with different concentrations of GCV. And bystander effect was also measured through mixed different concentrations of NCI-446 and NCI-446/TK.

Meanwhile, combining HSV-TK/GCV suicide gene system and sonodynamic therapy, cell survival rate was tested by MTT, in addition, cell cycle and apoptotic rate were tested by Flow cytometry. Results With 0.2 mg/L of GCV, the growth of NCI-446/TK was inhibited significantly ( $P < 0.01$ ). With increased GCV, the inhibitory effect became obviously. When 10% NCI-446/TK in mixed cells, there was 46% total cells were inhibited. And also the inhibitory effect increased with increasing proportion of NCI-446/TK. After therapeutic alliance with suicide gene system HSV-TK/GCV and SDT, cell survival ratio was significantly lower than the groups of single treatment and the proportion of cells in G0/G1 stage, as well as apoptotic rate, were also higher than the groups of single treatment. Conclusion The lethal effect of HSV-TK/GCV suicide gene system was enhanced with increase of GCV concentration and bystander effect was also significant. When combined with SDT, the effect was better than a single treatment group.

Key words: Suicide gene system Sonodynamic therapy Lung cancer cells Therapeutic alliance

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