



腺病毒介导的HSV-TK/GCV自杀基因治疗前列腺癌的体外实验

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Adenoviral Mediated HSV-TK/GCV Suicide Gene Transfer in Treatment of Prostate Cancer Cells *in Vitro*

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- 摘要
- 参考文献
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摘要 目的 以恶性肿瘤无限增殖特性为靶点, 应用人端粒酶逆转录酶启动子 (hTERT) 和小鼠巨细胞病毒启动子 (CMV) 调控携带 HSV-TK基因的减毒非增殖型腺病毒, 通过体外实验观察HSV-TK/GCV自杀基因疗法对前列腺癌细胞LNCaP, PC-3和人正常成纤维细胞MRC-5的治疗效果, 对其抗肿瘤机制进行初步探讨。方法 将腺病毒转染细胞后, 在荧光显微镜下观察绿色荧光蛋白的表达情况, 通过细胞病理效应 (CPE)、细胞活力实验 (MTT) 和电泳法检测Ad-hTERT-HSV/TK选择性杀伤肿瘤细胞。结果 Ad-hTERT-EGFP仅能转染肿瘤细胞, 而Ad-CMV-EGFP对正常和肿瘤细胞都能转染。细胞病理效应 (CPE) 发现Ad-hTERT-HSV/TK对肿瘤细胞具有很强的杀伤能力, 而对正常细胞无明显杀伤作用。细胞活力实验 (MTT) 量化地反映出Ad-hTERT-HSV/TK选择性杀伤肿瘤细胞。电泳法检测到, 在表达HSV/TK的肿瘤细胞出现细胞凋亡。结论 本实验利用由hTERT启动子调控EGFP报告基因的腺病毒, 证明了腺病毒的转染效果及重组病毒Ad-hTERT-HSV/TK具有选择性肿瘤细胞杀伤能力。

关键词: 前列腺癌 基因疗法 重组腺病毒 报告基因

Abstract: Objective To evaluate human prostate carcinoma cells as targets for herpes simplex virus thymidine (HSV-TK) mediated gene therapy, we tested the utility of adenoviral vectors on three human cell lines LNCaP, PC-3, and MRC-5. Our viral vectors carried a fusion gene of HSV-TK and an enhanced fluorescent protein for accurate

determination of the gene transfer rate and its contribution to the treatment results in each case.

Methods We use a recombinant adenovirus vector containing the enhanced green fluorescent protein (EGFP) gene. Cells transfected with recombinant adenovirus expressed green fluorescent protein. The percent of transfection was determined by fluorescence microscopy. To assay the cytolytic effects of Ad-hTERT-HSV/TK on tumor and normal cells, we performed a Cytopathic Effect test. MTT assay was used to determine cell viability at various GCV concentrations. DNA ladder assay was carried out to show the apoptosis of transferred cells.

Results Ad-hTERT-EGFP was observed to transfer efficiently in prostate cancer cells but poorly in normal cells under fluorescence microscope. Cytopathic Effect test and MTT assay showed that Ad-hTERT-HSV/TK selectively transferred and killed tumor cells while leaving normal cells unaffected. **Conclusion** Recombinant adenovirus vector containing EGFP can report percent of transfection correctly and conveniently. The human prostate cancer cells LNCaP is more sensitive to the treatment of AdTK/GCV system than PC-3. In summary, we demonstrate a new strategy for prostate cancer biotherapy and it has potential application in clinic.

Key words: Prostate cancer Suicide gene Recombinant adenovirus Report gene

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