

## 端粒双靶点抑制对肺癌细胞A549衰老的影响

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### Senescence Induced by Combination with Two Telomere-based Oligomers in Human Lung Adenocarcinoma A549 Cell Lines

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#### 摘要

#### 目的

观察两种端粒相关的反义寡核苷酸对人肺腺癌细胞A549形态、功能、凋亡及细胞传代的影响。

#### 方法

将培养的A549细胞随机分为空白对照组、端锚酶正义寡核苷酸对照组(sTANKS)、端粒酶催化亚单位正义寡核苷酸对照组(shTERT)、端锚酶反义寡核苷酸实验组(asTANKS)、端粒酶催化亚单位反义寡核苷酸实验组(ashTERT)、端锚酶及端粒酶催化亚单位反义寡核苷酸联合实验组(asTANKS+ ashTERT)，分别与不同的正、反义寡核苷酸作用，光学显微镜下观察细胞形态，细胞氯摄取率([3H]-TdR)监测细胞利用合成DNA的胸腺嘧啶的能力，β-半乳糖苷酶(X-Gal)转染效率评估细胞衰老状态下的应激能量代谢，hoechst33342荧光染色检测A549细胞凋亡，通过传代实验分析细胞寿命。

#### 结果

联合作用的两种反义寡核苷酸(ashTERT+asTANKS)能明显诱导A549细胞的衰老及凋亡，抑制DNA合成的含氯的胸腺嘧啶的摄取，增加细胞衰老状态的β-半乳糖苷酶(X-Gal)转染效率；并使A549细胞平均寿命明显缩短，在经过( $24.53 \pm 0.40$ )次倍增后发生传代终止，与单独作用的asTANKS或ashTERT相比均有明显的差异。

#### 结论

两种针对端粒的反义寡核苷酸的联合作用，使A549细胞从形态及功能上倾向于衰老、“去永生化”，有可能成为新的抗肿瘤药物靶点。

关键词：衰老 凋亡 人肺腺癌A549细胞 端粒 反义寡核苷酸

Abstract:

#### Objective

To evaluate the alteration in morphous and function for A549 cells, which induced by antisense tankyrase oligomers (asTANKS) combined with antisense human telomerase reverse transcriptase (ashTERT) oligomers and explore potential target of telomere-based molecular cancer therapeutics.

#### Methods

A549 cells was randomly assigned to 3 groups: ashTERT, ashTERT + asTANKS and asTANKS, while 3 groups (shTERT, sTANKS and blank) as control. With individual intervention for different hours, cells in morphous was observed by optical microscope, and proliferative activity evaluated by [3H-thymidine] uptake assay and X-Gal transfection test as well. Moreover, apoptosis body was measured by Hoechst 33342 fluorescence staining, and besides, duration of proliferation by population double

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test analyzed.

## Results

A549 cells was prone to senescence in morphous with asTANKS or ashTERT as passage time was delayed well and the trend combinated between asTANKS and ashTERT was more significant, in which apoptosis body appeared, Uptake rate in [<sup>3</sup>H]-TdR trend to suppression and transfection efficiency in X-Gal was enhanced gradually under continuous treatment with ashTERT or asTANKS, but combinated effect was more markedly. Certainly, population double times was shortened more rapidly with the combination of asTANKS and ashTERT, although the same effect was observed with single factor.

## Conclusion

In coordination with two telomere-based oligomers, A549 cells prone to come to the end more quickly, and it provides insight into strategies for telomere-based molecular cancer therapeutics.

Key words: **Senescence; Apoptosis; Human lung adenocarcinoma A549 cell lines; Telomere Antisense oligomers**

收稿日期: 2013-02-16;

基金资助:

湖北省卫生厅科研基金资助项目(2010Z-Y19)；武汉市人事局、武汉市卫生局科研基金资助项目(WX10AO3)

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引用本文:

卢宏达,孔庆志,雷 章等. 端粒双靶点抑制对肺癌细胞A549衰老的影响[J]. 肿瘤防治研究, 2013, 40(05): 434-438.

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[J]. Cancer Research on Prevention and Treatment, 2013, 40(05): 434-438.

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