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论著

塞替派诱发人支气管上皮恶性转化成瘤细胞的基因突变

周 喆*，袁素波，廖明阳

(军事医学科学院毒物药物研究所, 北京 100850)

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摘要 目的 旨在了解转化细胞在成瘤过程中的*p*15，*p*16，*p*53和*K-ras*基因编码序列突变情况。方法 运用逆转录聚合酶链反应（RT-PCR）技术和DNA测序技术。结果 转化各阶段细胞*p*15和*K-ras*基因编码序列为野生型。在转化进程中，各转化细胞均携带与细胞永生化有关的*p*53第47密码子CCG→TCG(脯氨酸→丝氨酸)转换，在此基础上无新的错义突变发生。*p*16基因在BEAS-2B细胞和BEAS-STE细胞中均为野生型，在BEAS-TTb细胞中第4密码子发生TCG→TAG(丝氨酸→
终止密码子)碱基转换，结果为无义突变，第19，52密码子分别发生GAG→AAG(谷氨酸→赖氨酸)转换，GCG→ACG(丙氨酸→苏氨酸)转换的错义突变。BEAS-TTc细胞中第19密码子发生GAG→AAG(谷氨酸→赖氨酸)转换的错义突变，而没有可检测的BEAS-TTa细胞的mRNA存在。结论 *p*16基因的突变或表达缺失与恶性转化细胞的成瘤过程相关。

关键词 塞替派 上皮细胞, 支气管, 人 基因, p15 基因, p16 基因, p53 基因, K-ras 细胞转化, 肿瘤 突变

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Gene mutation in the tumorigenic transformation process of immortalized human bronchial epithelial cells induced by thiotepa

ZHOU Zhe*, YUAN Su-Bo, LIAO Ming-Yang

(Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences, Beijing 100850, China)

Abstract

AIM To understand the molecular mechanisms involved in progressive tumorigenesis. **METHODS** Reverse transcription polymerase chain reaction was utilized to generate the total protein coding region cDNA of *p*15, *p*16, *p*53[and *K-ras* gene which were sequenced for mutation. **RESULTS** BEAS-2B, BEAS-TE and BEAS-TT cells were used to detect the mutation of *p*53. The result disclosed codon 47 CCG→TCG transversion of all the five cell lines, which is responsible for the immortalization of BEAS-2B cell. There was no other cumulative missense mutation detected at *p*53 gene in the BEAS-TT cell lines. Protein coding region of *p*15 and *K-ras* gene was all wild type for all the five cell lines. For BEAS-2B and BEAS-TE cell, the cDNA of *p*16 gene was a wild type, while a non- sense mutation in the condon 4(TCG→TAG) and missense mutation in the codons 19,52(GAG→AAG, GCG→ACG) were demonstrated in the BEAS-TTb cell. For BEAS-TTc, there was one missense mutation in codon 19(GAG→AAG). There was no detectable mRNA of *p*16 gene expression in the BEAS-TTa. **CONCLUSION** Mutation of *p*16 gene may be mechanistically related to thiotepa induced malignant transformation.

Key words thiotepa epithelial cells bronchial human genes p15 genes p16 genes p53 genes K-ras cell transformation neoplastic mutation

DOI:

通讯作者 周 喆 zhouzhe76@yahoo.com.cn