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非小细胞肺癌PTEN基因突变的临床特征

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Characteristics of PTEN Mutation Status in Patients with Non-small Cell Lung Cancer

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摘要

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摘要 了解非小细胞肺癌中PTEN基因突变的分布状况及其临床特征。方法：选取2003年9月至2009年12月间182例在广东省人民医院收治的非小细胞肺癌患者的手术或穿刺标本，抽提RNA后，逆转录成cDNA，再进行PCR扩增PTEN 1～9外显子及EGFR 18～21外显子，用直接测序法检测基因突变。结果：182例标本中，PTEN基因的突变率为9.9%（18/182），PTEN基因的突变率女性为6.5%，男性为11.0%（P=0.549）；吸烟者为13.0%，非吸烟者为6.7%（P=0.15）；腺癌为7.8%，鳞癌为9.9%（P=0.628），差别均无统计学意义。常见的突变类型有点突变、插入突变及缺失突变，共11例，主要分布在第8外显子，也可见于第4、5、9外显子；其中10例为男性吸烟者，1例为男性非吸烟者；8例为鳞癌，1例腺癌，2例大细胞癌；此外，发现7例大片段缺失突变，缺失片段位于第1～7外显子，约250～539 bp碱基丢失，突变率为3.8%（7/182），除了1例为大细胞癌外，其余6例均为腺癌；PTEN基因突变率与性别、吸烟状态分布无统计学相关性；其中4例大片段缺失伴随EGFR基因敏感突变。结论：具有不同PTEN基因突变类型的NSCLC可能是两种不同的疾病类型，不同突变类型的PTEN基因在NSCLC中的作用机制不同。PTEN基因的大片段缺失可能是突变型EGFR对TKI原发耐药的原因之一。

关键词： 非小细胞肺癌 PTEN 基因突变 直接测序 临床特征

Abstract: To detect and investigate the somatic mutations of the phosphatase and tensin homolog deleted on chromosome ten (PTEN) in patients with non-small cell lung cancers (NSCLCs). Methods: DNA and RNA were isolated from 182 tumor tissues obtained from the tumor bank of the Guangdong Lung Cancer Institute. The sequences of exons 1 to 9 of the PTEN gene and exons 18 to 21 of EGFR were assayed using PCR and direct sequencing. The relationships of the PTEN mutation rate with the clinical parameters were analyzed using Fisher's exact test. A two-tailed P-value of <0.05 was considered statistically significant.Results: Eighty-one of the 182 patients had squamous cell carcinoma, 90 with adenocarcinoma, and 11 with large cell carcinoma. PTEN mutations were present in 18 (9.9%) of the 182 tumors. These mutations were observed as follows: male and female at 11.0% and 6.5% (P = 0.549), respectively; smokers and non-smokers at 13.0% and 6.7% (P = 0.15), respectively; and in patients with adenocarcinoma and squamous cell carcinoma at 7.8% and 9.9% (P = 0.628), respectively. No significant differences were observed between these mutations. PTEN mutation types were predominantly point mutation, small fragment deletion, and insertion mutation. These mutations were primarily present in exon 8. Ten mutations were all found in males and in smokers, in addition to one mutation in males and in non-smokers. However, 7 large fragment deletion mutations were found, 6 of which were in ACs. The mutation rate was 3.8% (7/182). The deleted fragments were approximately 250 to 539 bases and primarily present in exons 1 to 7. No significant relationships were observed between the large fragment deletion and gender as well as smoking habits. We found 4 large fragment deletions coupled with EGFR activating mutations. Conclusion: NSCLC with different types of PETN mutation may represent two different diseases. Large deletion mutations of PTEN may contribute to resistance to EGFR TK inhibitors in patients with mutant EGFR.

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