Rapid detection of hotspot mutations in epidermal growth factor receptor by polymerase chain reaction facilitates the management of non-small cell lung cancer

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摘要

Abstract

Purpose: A positive response to gefitinib in non–small cell lung cancer (NSCLC) has been correlated to mutations in epidermal growth factor receptor (EGFR) gene. Previous reports have been based mainly on diagnostic screening by sequencing. However, sequencing is a time-consuming and complicated procedure, not suitable for routine clinical use.

Experimental Design: We have developed rapid, simple, and sensitive mutation detection assays based on the SMart Amplification Process (SMAP) and applied it for analyzing EGFR gene mutations in clinical samples. By using SMAP, we can detect mutations within 30 min including sample preparation. To validate the assay system for potential use in clinical diagnostics, we examined 45 NSCLC patients for EGFR mutations using sequencing and SMAP.

Results: The outcomes of the SMAP assay perfectly matched the sequencing results, except in one case where SMAP was able to identify a mutation that was not detected by sequencing. We also evaluated the sensitivity and specificity of SMAP in mutation detection for EGFR. In a serial dilution study, SMAP was able to find a mutation in a sample containing only 0.1% of the mutant allele in a mixture of wild-type genomic DNA. We also could show amplification of mutated DNA with only 30 copies per reaction.

Conclusions: The SMAP method offers higher sensitivity and specificity than alternative technologies, while eliminating the need for sequencing to identify mutations in the EGFR gene of NSCLC. It provides a robust and point-of-care accessible approach for a rapid identification of most patients likely to respond to gefitinib.