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# Lung alert

## A non-invasive technique to genotype lung cancer cells

Mutations in the epithelial growth factor receptor (EGFR) are thought to occur early in the oncogenesis of non-small cell lung carcinoma (NSCLC). This paper describes the use of a novel chip to capture circulating tumour cells (CTCs) combined with a "SARMS" (Scorpion Amplification Refractory Mutation System) allele-specific genotyping assay to detect EGFR mutations.

The study used blood samples, radiological measurements and tumour biopsy specimens from a group of 46 patients with NSCLC. In a sample of 23 patients the chip and SARMS combination showed high sensitivity and specificity in detecting EGFR mutations, correlating with standard polymerase chain reaction (PCR) on biopsy specimens. The recently described free plasma DNA analysis method was less sensitive in comparison. Analysis of subgroups also revealed some interesting correlations. Although absolute CTC cell numbers correlated poorly with radiological tumour size, serial measurement of the above two parameters show good correlation with disease progression. The SARMS assay also detected the T790M drug resistance mutation whose prevalence was increased after the initiation of monoclonal antityrosine kinase therapy and whose presence was associated with a poorer prognosis.

The dynamic nature of the tumour response to therapy means monitoring for the emergence of resistant cell clones can aid genotype-targeted therapy, as opposed to treatment based on the initial biopsy result alone. Tailored therapy represents a paradigm shift away from generic chemotherapy and may lead to more efficient use of resources. This is a promising non-invasive test, but there are practical considerations before it can be applied to clinical practice.

► Maheswaran S, Sequist LV, Nagrath S, *et al*. Detection of mutations in EGFR in circulating lung-cancer cells. *N Engl J Med* 2008;**359**:366–77

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