

# EGFR Mutation Detection by PCR and Fragment Analysis

## FOR PREDICTION OF RESPONSE TO EGFR INHIBITORS IN NON-SMALL-CELL LUNG CANCER

### Clinical Background

- Lung cancer is the second most common cancer and the most common cause of cancer-related death in both men and women in the United States.<sup>1</sup>
- Somatic mutations in the kinase domain of *EGFR* have been reported in a subset of lung cancer patients with non-small-cell lung cancer (NSCLC).<sup>2</sup>
- Multiple studies have illustrated that *EGFR* mutations are closely associated with tumor response and clinical outcome in patients with NSCLC who are receiving treatment with the *EGFR* tyrosine kinase inhibitors gefitinib or erlotinib.<sup>4</sup>
- The mutational status of *EGFR*, in particular the presence or absence of the exon 19 deletions and L858R point mutation in exon 21, is a strong predictor of the sensitivity of *EGFR* tyrosine kinase inhibitors.

### Genetics

- Although several *EGFR* mutations have been identified, they are reported to be concentrated in exons 18–21 of *EGFR*.
- Two mutations account for ~90 percent of *EGFR* mutations reported to date in lung adenocarcinoma.<sup>3</sup> The most common mutation, seen in ~46 percent of cases with *EGFR* mutations, is a short in-frame deletion of 9, 12, 15, 18, or 24 nucleotides in exon 19. The second most common mutation, seen in ~43 percent of cases with *EGFR* mutations, is a point mutation in exon 21: the 2573T>G substitution, which indicates the L858R mutation.<sup>3</sup>

### Indications for Ordering

The principal use for this test is to detect the presence of *EGFR* mutations in NSCLC. This test is not intended to detect minimal residual disease.

### Methodology

- Genomic DNA extracted from formalin-fixed, paraffin-embedded tissue is subjected to PCR amplification of *EGFR* exons 19 and 21.
- Exon 21 amplicons are enzymatically purified and digested with Sau96I. Exon 19 and 21 amplicons are then analyzed by capillary electrophoresis on the ABI-3100.
- Sensitivity: The limit of detection for exon 19 and exon 21 is 20 percent tumor cells

### Interpretation

- Exon 19 not detected: An exon 19 mutation was not detected.
- Exon 21 not detected: The L858R mutation was not detected.
- Exon 19 positive: An exon 19 deletion was detected.
- Exon 21 positive: The L858R mutation was detected.

### Limitations

- Results of this test must always be interpreted in the context of morphologic and other relevant data, and should not be used alone for a diagnosis of malignancy.
- A negative result does not preclude the presence of an *EGFR* mutation in exons 18 and 20 or 19 and 21 below the limits of detection.

### Related Test

*EML4/ALK* Translocation by RT-PCR (2004547)

### References

1. Jemal A, et al. Cancer statistics. *CA Cancer J Clin* 2007;57:43–66.
2. Lynch TJ, et al. Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib. *N Engl J Med* 2004;350(21):2129–39.
3. Pan Q, Pao W, Ladanyi M. Rapid polymerase chain reaction-based detection of epidermal growth factor receptor gene mutations in lung adenocarcinomas. *J Mol Diagn* 2005;7(3):396–403.
4. Han SW, et al. Predictive and prognostic impact of epidermal growth factor receptor mutation in non-small-cell lung cancer patients treated with gefitinib. *J Clin Oncol* 2005;23(11):2493–501.
5. Jänne PA, Engelman JA, Johnson BE. Epidermal growth factor receptor mutations in non-small-cell lung cancer: implications for treatment and tumor biology. *J Clin Oncol* 2005;23(14):3227–34.

## Test Information

**2002440**

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For information on test selection, ordering, and interpretation, refer to ARUP Consult® at [www.arupconsult.com](http://www.arupconsult.com).