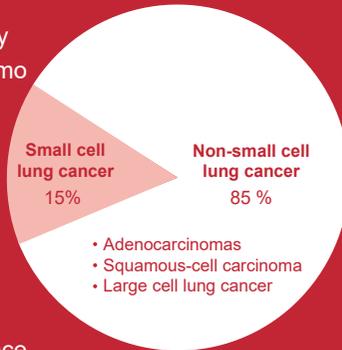


## Non-Small Cell Lung Cancer

About 85% of lung cancer is non-small cell lung cancer. Among this, adenocarcinomas (including alveolar cell carcinoma) is the most common one, especially in women and non-smoker. Squamous-cell carcinoma occurs in bigger respiratory track, causing cough and hemoptysis. It will also block the respiratory track, resulting in wheezing and obstructive pneumonia<sup>1</sup>.

### Characteristics

- Grow and transfer slowly
- Not sensitive to the chemo and radiation therapies, should do the surgery earlier to cure
- Patients with mediastinal lymph node metastasis will have higher risk of metastasis and recurrence



### CTCatch™ Clinical Applications in Lung Cancer

1 2 3

#### Diagnosis

- TTF1

#### Monitoring

- EGFR mutation
- CSV

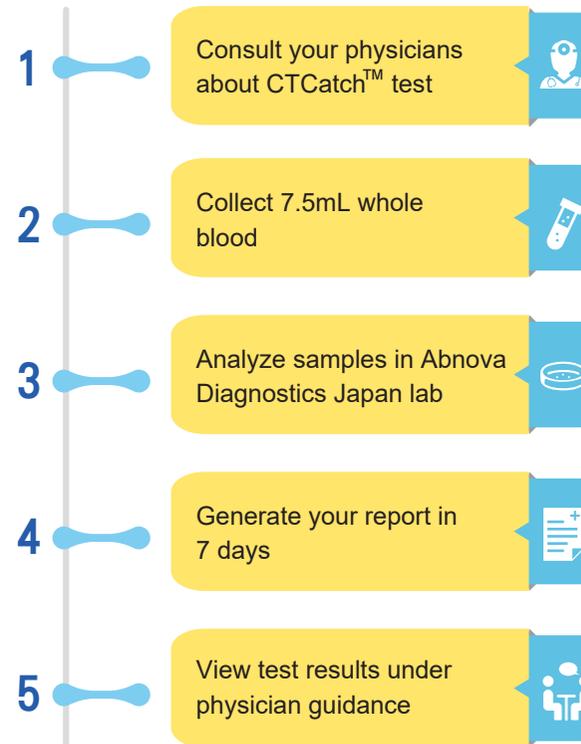
#### Treatment

- EGFR-TKI
- PD-1 inhibitor

Consult your physicians about CTCatch™ test.



## CTCatch™ Test Process



## CTC Liquid Biopsy for Non-Small Cell Lung Cancer

Abnova Diagnostics Japan  
CTCatch™ Test



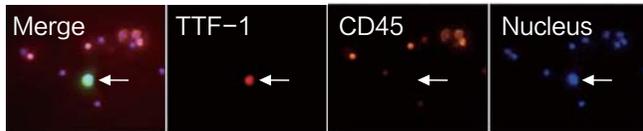
Address: National Cancer Center Research Institute  
3F, 5 Chome-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan  
Tel: + 81 3 6264 3448 Fax: + 81 3 6264 3449  
[www.abnovadx.com](http://www.abnovadx.com)

# 1 Diagnosis

## TTF1

Thyroid transcription factor-1 (TTF-1) is a tissue specific transcription factor expressed in epithelial cells of the thyroid and lung. One recent study has shown that<sup>2</sup>:

- TTF-1 antibody can be used to distinguish primary lung adenocarcinoma and other adenocarcinomas.
- Due to its high specificity, TTF-1 is a immunohistochemical marker in the diagnostics of primary lung adenocarcinoma.
- Clinically, TTF-1 positive circulating tumor cells (CTCs) from cancer patient with metastasis can be used to identify cancer cell origin.

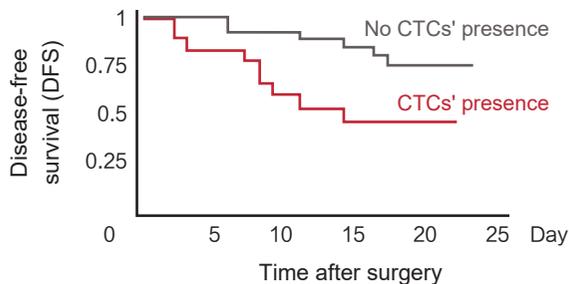


CTCcatch™ detects TTF-1 positive cells (human lung cancer cell line PC9).

# 2 Monitoring

## Recurrence

Epidermal growth factor receptor (EGFR) overexpression is found in 40-80% of NSCLC patients. Research indicated that the presence of CTCs after surgery was significantly associated with early recurrence and shorter disease free survival (DFS)<sup>3</sup>.



According to CTC status one month after surgery, patients with CTC presence had shorter DFS than patients without CTC presence.

## Metastasis

CTCs are associated with metastatic progression and prognosis. In addition, epithelial-mesenchymal transition (EMT) is a critical stage in metastasis. CTCs in patients with late metastatic NSCLC have been characterized<sup>4,5</sup>:

- Most cancer cells are with epithelial-mesenchymal phenotype.
- Some cancer cells are only with mesenchymal phenotype marker, such as cell-surface vimentin (CSV).
- Metastatic cancer cells with EMT phenotype are involved in drug resistance.

Characterization of CTCs with an epithelial/mesenchymal phenotype provides further insight into the mechanism of NSCLC metastasis.

# 3 Treatment

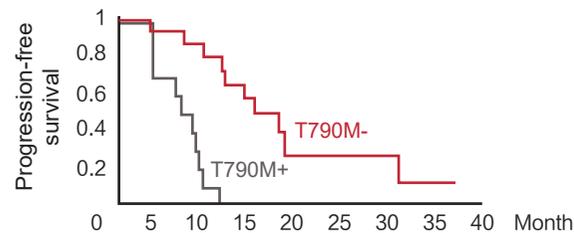
## TKI Drug Resistance<sup>6,7</sup>

First Generation

"Classical" mutation is the most common epidermal growth factor receptor (EGFR) mutation in NSCLC, including exon 19 deletion and exon 21 point mutation L858R. Epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) is one of the most common NSCLC drugs. EGFR mutation is used to identify NSCLC patients who can benefit from EGFR-TKI therapy.

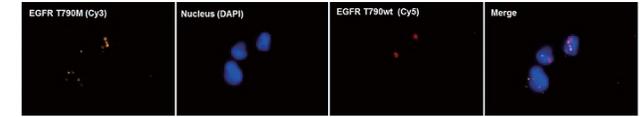
Second Generation

One year after taking the first generation EGFR-TKI, most patients will suffer from secondary mutation with methionine replacing threonine at T790M. The mutation causes drug resistance so that the second generation therapy is needed.



Correlation between the presence of T790M mutations in tumors and progression-free survival

To detect gene mutations, Abnova Diagnostics Japan has developed mutaFISH™ probes which allow on-chip, *in-situ* mutation analysis of CTCs, and directly detect the gene mutations.



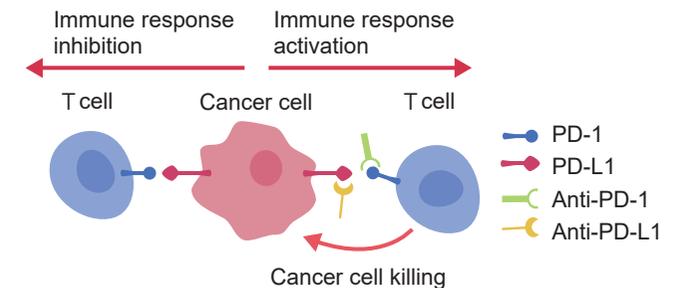
mutaFISH™ probes detect the presence of EGFR T790M mutations in human lung cancer cell line (H1975).

## PD-1/PD-L1 Immunotherapy

Programmed cell death protein 1 (PD-1) and its ligand, PD-L1, are responsible for immune response. According to the recent research<sup>8</sup>:

- Induced PD-L1 inhibits the immune response to cancer cells and leads to deterioration and metastasis.
- PD-L1 expression ranges from 45 to 50% in NSCLC biopsies, causing poor clinical outcome.
- Anti-PD-1/PD-L1 therapy activates immune response and kills cancer cells.

CTCcatch™ detects the expression of PD-L1 in cancer cells offering physicians more therapeutic options for clinic.



## Reference

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