Nature Reviews Clinical Oncology advance online publication 28 May 2013; doi:10.1038/nrclinonc.2013.89

LUNG CANCER

ALK status of NSCLC reflected in CTCs

Lung cancer is the leading cause of cancer death worldwide, with non-small-cell lung cancer (NSCLC) accounting for the majority of cases. The discovery that the EML4–ALK fusion protein kinase is a potent oncogenic driver in 3–7% of patients with NSCLC led to the development of the ALK inhibitor crizotinib. This agent and an accompanying companion diagnostic test were granted FDA approval for the detection of *ALK*-rearrangements. The test is performed on tumour biopsies or fine-needle aspirates, but is hampered by the lack of available tumour tissue.

A group led by Françoise Farace has evaluated whether circulating tumour cells (CTCs) might represent a noninvasive source of tumour material in NSCLC. Researchers isolated CTCs from 32 patients with metastatic NSCLC, 18 of whom had *ALK*-positive tumours. Farace explains: "Because cell number is an essential criterion to exploit CTCs ... we focused on the development of a fluorescence *in situ* hybridization (FISH) method on filters (Filter Adapted-FISH, FA-FISH) that takes into account the very fragile nature of CTCs and allows high cell recovery."

ALK rearrangements were found in CTCs from all the patients with *ALK*-positive tumours. These CTCs had a unique *ALK* rearrangement and a mesenchymal phenotype, in contrast to the heterogeneous epithelial/mesenchymal phenotypes in the patient's tumours. Farace concludes, "*ALK*-rearranged CTCs could result from a clonal selection process of tumour cells displaying migratory and invasive properties, and possibly a higher metastatic potential. CTCs could represent a unique compartment to identify tumour clones that should be targeted by personalized treatments, as well as biomarkers that are more relevant for treatment prediction."

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Original article Pailler, E. *et al*. Detection of circulating tumor cells harboring a unique ALK rearrangement in ALK-positive non–small-cell lung cancer. *J. Clin. Oncol.* doi:10.1200/JCO.2012.44.5932