Liquid Biopsy for EGFR Lung Cancer

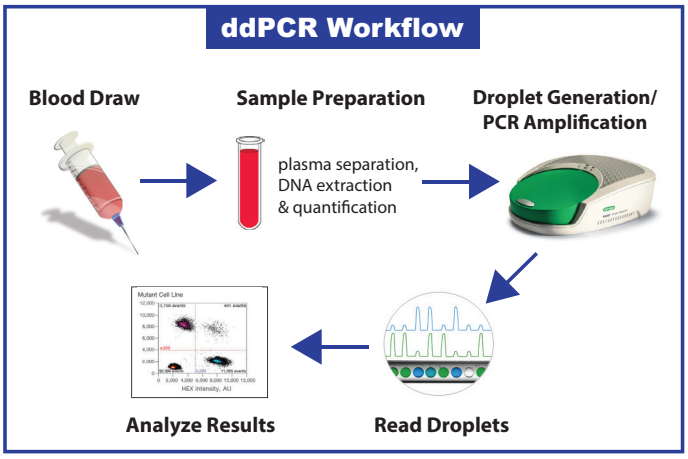
GOPATH® LABORATORIES
Global Pathology Services

"By detecting EGFR mutations, we can better predict lung cancer recurrence and resistance to targeted therapies such as TKIs."

Approximately 10-20% of patients with NSCLC have been found to have a mutation of the EGFR gene.[3]

EGFR and Lung Cancer

Lung cancer is the leading cause of cancer-related deaths in the United States[1], with Non-Small Cell Lung Cancer being the most common type of lung cancer diagnosed[2]. In fact, NSCLC accounts for roughly 85% of all lung cancers[2]. Approximately 10-20% of patients with NSCLC are found to have a mutation of the epidermal growth factor receptor (EGFR) gene[3]. EGFR is a tyrosine kinase receptor that exists on the surface of each cell. When it mutates, it causes the tyrosine kinase protein to become overactive, leading to the uncontrolled growth of cancer cells. Identifying EGFR mutations can help clinicians to better assess which treatment options will work best when treating their patient's cancer, such as therapies that specifically target EGFR overexpression (tyrosine kinase inhibitors, commonly called TKIs). Detecting EGFR mutations also helps predict lung cancer recurrence as well as indicates a tumor's likely resistance to certain therapies, which may limit options when considering which treatment to choose.



Clinical Utility

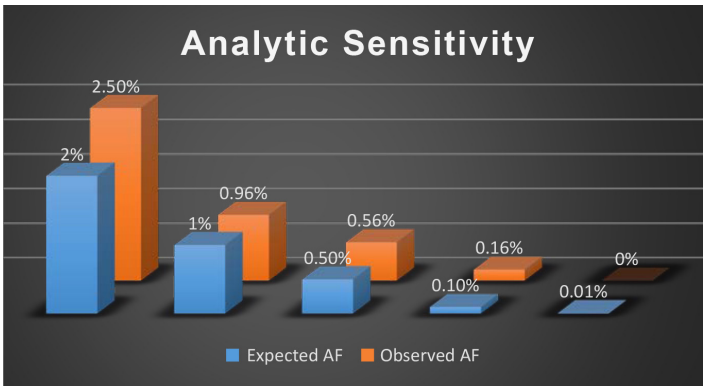
When tumor cells die off, they enter the bloodstream, carrying valuable genetic information with them. Recent advancements have made it possible to examine this circulating tumor DNA (ctDNA) through a simple blood draw, giving us insight into how a cancer is progressing without the need for additional tissue biopsies. This can be helpful when a tissue sample may be difficult to obtain due to the location of the tumor, the fragility of the patient's health, or if there isn't enough tissue left from an initial biopsy to perform additional tests. As a cancer grows and changes, old tissue samples may no longer contain relevant information. Liquid biopsy makes it possible to monitor a cancer's growth and its responsiveness to treatments in real time without having to rely on old data or needing to perform additional tissue biopsies. Liquid biopsy may also complement tissue biopsies by providing clinicians with potentially-actionable mutations and targeted therapies[4]. Liquid biopsy may also make it possible to detect the recurrence of cancer sooner than traditional methods.

Assay Description and Methodology

Plasma is separated by centrifugation from whole blood samples collected in EDTA tubes. Cell-free DNA (cfDNA) is extracted from each plasma collection using MagMAX™ Cell-Free DNA Isolation Kit (Thermo Fisher Scientific), and is quantified by Qubit Fluorometric Quantitation (Thermo Fisher Scientific). For each sample, exon 19 deletion, and exon 18 c.2155G>A (G719S), exon 20 c.2369C>T (T790M), exon 21 EGFR c.2573T>G (L858R) & c.2582T>A (L861Q) mutations for non-small cell cancer in the EGFR gene are analyzed by a digital PCR approach using assay reagents and a QX200 digital PCR System from BioRad Inc. The sensitivity cut-off established by our laboratory for the detection of these mutations ranges from 0.1-0.5%.

EGFR Liquid Biopsy and ddPCR

This ddPCR test has an advantage over other technology by providing tens of thousands of data points from a single sample, rather than a single result from one sample. The blood sample is partitioned into 20,000 droplets with target and background DNA randomly distributed among the droplets. After PCR amplification, each droplet provides a fluorescent positive or negative signal indicating the target DNA was present or not present after partitioning. Each droplet gives us an independent digital measurement. As a result, ddPCR allows for absolute quantification, unparalleled precision and higher overall testing accuracy, giving clinicians the most accurate results for detecting EGFR mutations and monitoring a patient's cancer in real time.



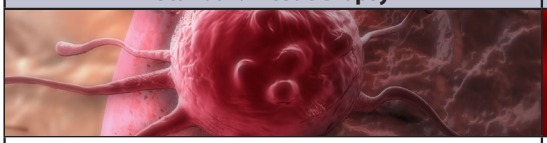
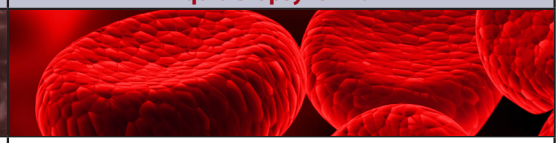
EGFR and Targeted Therapies

NSCLC patients with EGFR mutations have been found to be more responsive initially to TKIs. These drugs prevent the activation of the EGFR signaling pathways and thus slow cancer cell growth. Since normal cells are not affected by targeted therapies, patients often experience fewer side effects than they do with standard chemotherapy. Erlotinib (Tarceva), Gefitinib (Iressa) and Afatinib (Gilotrif) are all examples of EGFR-inhibiting drugs. Studies have shown that patients with EGFR mutations who received TKIs were found to have higher response rates than patients treated with standard chemotherapy[5]. However, many NSCLC tumors develop mutations that eventually make them TKI-resistant[6]. Liquid biopsy can be a vital tool for monitoring tumor progression and identifying new mutations or therapy resistance. Performing subsequent liquid biopsy tests throughout a patient's treatment can help clinicians continue to monitor cancer's progression, as well as detect the tumor's responsiveness to targeted therapies without having to perform additional invasive and oftentimes risky biopsies.

Samples for Submission

Collect 15mL of peripheral blood and place in an EDTA tube. Use cold pack for transport, making sure cold pack is not in direct contact with specimen. Ship sample within 24 hours of blood draw. If you must ship the sample for a late Friday or weekend delivery, please call us to make special arrangements.

Standard Biopsy/Liquid Biopsy Comparison

Standard Tissue Biopsy	Liquid Biopsy for EGFR
	
Invasive procedure that could compromise patient health	Can be performed from a minimally invasive blood draw
Sample not always easy to obtain due to tumor location	Sample easily obtained
Painful procedure that carries some risk	Minimal pain/risk
Time-intensive procedure	Quick turnaround (TAT) and recovery
Only part of tumor that was biopsied is analyzed	Comprehensive tissue profile completed

References

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