Bristol Genetics Laboratory is a UKAS accredited medical laboratory No.9307.

Genetic Testing in Lung Cancer

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Sample Required

Paraffin embedded tumour tissue

- **>20% tumour:** 5 x 10um sections in a clean universal
- **<20% tumour**: 10 x 5um slide mounted sections along with H&E with regions of >20% tumour highlighted

Samples should be accompanied by a FULLY completed Molecular Pathology request form (available from the laboratory or www.nbt.nhs.uk/genetics)

All samples should be labelled with patient name, date of birth and pathology block number

Consent and Storage:

All genetic testing requires consent. **It is the responsibility of the referring clinician to ensure that appropriate consent has been obtained.**

DNA is stored from **ALL** patients undergoing DNA testing, unless consent for this is specifically denied.

Stored material from all referrals may be retained for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Clinical Background and Genetics

EGFR, ALK, BRAF, KRAS, PIK3CA and ERBB2 mutation analysis is available at BGL for Non-Small Cell Lung Cancer (NSCLC) patients to guide targeted inhibitor therapy, clinical trial eligibility and diagnosis.

EGFR

Approximately 10% of NSCLC patients have a mutation in the *EGFR* gene which can be targeted with *EGFR* Tyrosine Kinase Inhibitors (TKI). The panel used detects over 99% of all known *EGFR* tyrosine kinase domain mutations in NSCLC, including both activating mutations and resistance mutations.

ALK

ALK rearrangements are detected in approximately 5% of NSCLC patients and can be targeted with TKI therapies. BGL offers an *ALK* FISH service which is used to confirm or clarify positive or equivocal ALK protein expression results using immunohistochemistry.

BRAF

BRAF mutations are detected in up to 4% of NSCLC; the most common mutation being p.(Val600Glu) (V600E), however non V600E mutations are more common in lung cancer than other tumour types. Phase II trials have shown that BRAF and MEK inhibitors could offer a targeted therapy to patients with *BRAF* V600E mutant NSCLC.

KRAS

KRAS mutations are a common driver in NSCLC (15-25% patients) and are generally associated with a poorer prognosis. *KRAS* mutations do not overlap with *EGFR* mutations, *ALK* rearrangements or *ROS1* rearrangements.

PIK3CA

PIK3CA mutations occur in approximately 1% of NSCLC, more frequently in tumours of squamous histology. There are agents in clinical trials for which *PIK3CA* mutation is an inclusion criterion.

***ERBB2* (HER2)**

ERBB2 is mutated in up to 4% of NSCLC patients; the most common mutation is an insertion within exon 20. Anti-HER2 therapies are being investigated in clinical trials in NSCLC patients with an *ERRB2* exon 20 insertion or mutation.

Service Offered

Solid Tumour Next Generation Sequencing (NGS) Panel with analysis restricted to lung cancer genes (Illumina TruSight Tumour 15 assay). Regions covered are: *EGFR* exons 18, 19, 20 and exon 21 (p.848 to p.875); *BRAF* exon 15 (p.581 to p.605); *PIK3CA* exons 9 and 20; KRAS exon 2 (p.1 to p.20), exon 3 (p.38 to p.72) and exon 4; *ERBB2* exon 14 (p.551 to p.579), exon 17, exon 20 (p.770 to p.812), exon 21 (p.832 to p.864). This assay can detect a mutation at minimum 5% allele frequency in a background of wild type DNA.

***ALK* FISH** Abbott Molecular *ALK*, dual colour, breakapart probe used to detect clinically significant rearrangements at 2p23 involving *ALK*.

Referrals

Referrals are accepted from Consultant Oncologists, Respiratory Consultants or Consultant Histopathologists. For sample requirements please refer to the information on the left.

Target Reporting Times

Maximum 14 calendar days.

Quality

BGL participates in the *GENQA* scheme for this service.

References

Thomas, A. et al. Refining the treatment of NSCLC according to histological and molecular subtypes. Nat. Rev. Clin. Oncol. 12, 511–526 (2015)
NCCN Clinical Practice Guidelines in Oncology Non-Small Cell Lung Cancer version 7.2019
Planchard, D. et al. Dabrafenib plus trametinib in patients with previously untreated BRAFV600E-mutant metastatic non-small-cell lung cancer: an open-label, phase 2 trial. Lancet Oncol. 2017 Oct;18(10):1307-1316.

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