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

Genetic Testing in GIST

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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

- Gastrointestinal Stromal Tumours (GISTs) are the most common mesenchymal tumour of the gastrointestinal tract and are believed to arise from the interstitial cells of Cajal or their precursors[1].
- Activating mutations in the receptor tyrosine kinases *KIT* or *PDGFRA* are the hallmark of Gastrointestinal Stromal Tumour (GIST) diagnosis and predict response to tyrosine kinase inhibitor (TKI) therapy.
- *KIT* and *PDGFRA* are mutated in ~85% and ~5%, respectively, of GIST, leading to constitutive activation of the mutated kinase[1-3].
- Specific mutations can predict the response of primary GIST or secondary resistant tumours to TKI therapy e.g. imatinib or sunitinib, and also direct TKI drug choice or dose[1-3].
- *KRAS*, *NRAS* and *BRAF* mutations have been identified in a small proportion of GIST.

Service Offered

- Solid tumour Next Generation Sequencing (NGS) panel with analysis restricted to genes relevant to GIST (Illumina TruSight Tumour 15 assay). Regions covered are: *KIT* exons 8, 9, 10, 11, 13, 14, 17, 18, PDGFRA exons 12, 14 and 18, *BRAF* codons 581-605; *KRAS* codons 1 to 20, codons 38 to 72, exon 4; *NRAS* codons 1 to 22, codons 56 to 94, exon 4.
- This assay can detect a mutation at minimum 5% allele frequency in a background of wild type DNA.

Referrals

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

Target Reporting Times

- 14 days maximum.

Quality

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

References

1. Maki, R., V. Keedy. 2015. Molecular Profiling of Gastrointestinal Stromal Tumor (GIST). My Cancer Genome https://www.mycancergenome.org/content/disease/gist/
2. Rammohan *et al* 2013. A gist of gastrointestinal stromal tumors: A review. World J Gastrointest Oncol 2013 June 15; 5(6): 102-112.
3. Corless *et al* 2011. Gastrointestinal stromal tumours: origin and molecular oncology. Nature Reviews Cancer 11, 865-878.
4. NICE guidance: TA86, TA209, TA326

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