NHS
South West
Genomic Laboratory Hub

The SW GLH genetic testing service for solid tumours:

A guide for Cellular Pathologists

1. Introduction

- The SW Genomic Laboratory Hub (SWGLH) was implemented in 2018 to deliver genetic and genomic analyses for all patients with cancer and rare disease across the SW region.

- The SWGLH is a centralised service established as a partnership between North Bristol NHS Trust (NBT) and the Royal Devon and Exeter NHS Foundation. All cancer genetic services will be delivered from NBT.

- The SWGLH is part of a network of seven English GLHs established to drive the standardisation and rapid uptake of new genomic services and technologies and to ensure equity of patient access.

- This document provides guidance to NHS Pathology services to facilitate access to the cancer genetic testing services.

2. What cancer genetic test technologies are available at the SWGLH?

- The indications and test technologies for the SWGLH cancer genetic testing service are defined in a National Genomic Test Directory (NGTD) that is available at: https://www.england.nhs.uk/publication/national-genomic-test-directories/

- The NGTD will be regularly updated through an expert panel and peer review process based on advances in best clinical practice and scientific knowledge. We anticipate expansion of the NGTD to include many additional genes for existing tumour types, and additional tumour types for gene panel analysis. For instance, for existing tumour types, we expect inclusion of additional gene targets such as the tumour agnostic biomarkers NTRK1,2 & 3 during 2020-21.

Gene panel analyses

- There will be phased implementation of gene panel testing from April 2020. After this most cancer genetic tests will be provided by large gene panel analyses in which each tumour sample will be sequenced for approximately 500 genes (TSO500 panel).

- For each tumour type, genes for analysis and reporting back to the clinical team will only be those that influence current standard of clinical care, those linked to treatments expected to be approved imminently and those that inform eligibility or stratification in clinical trials.
  e.g. for NSCLC, the gene panel will provide information on EGFR, ALK fusions and ROS1 fusions (standard of care tests) and also BRAF, KRAS,

NTRK1,2 & 3 fusions, RET fusions, MET amplifications, MET skipping, PIK3CA, HER2, ALK mutations

- The selection of which genes will be analysed for each tumour type is currently being determined through national discussions between GLH cancer leads and oncology experts and will be reviewed on an ongoing basis.

Direct mutation tests

- In addition to large gene panel analysis, there are some tumour types and genes that will be analysed as a single gene test. This reflects the need for different technologies to be used to detect some gene variants, or for a cost-effective approach to be taken for common variants.

- The results from gene panels and single tests for a single patient will be combined and reported together.

Whole genome sequencing

- A small number of tumour types will have WGS performed. The current WGS cancer indications are sarcoma, paediatric tumours and acute leukaemia. WGS is currently expected to begin in mid-2020.

- In order to ensure timely return of clinically actionable genetic test results, rapid gene panel testing, or direct mutation analysis may also be performed on these samples in parallel with WGS. Dual testing will be reviewed as turnaround times for the national WGS service matures.

3. Which tumour types are eligible for analysis?

- The ultimate aim of the cancer genetic testing service within the GLH network is to provide a clinically relevant molecular profile for all tumour types at diagnosis and again in the event of relapse.

- This will be achieved through a phased implementation of new testing services at the SWGLH from April 2020, beginning with the application of new large panel analyses for tumour types for which genetic testing is already part of NHS standard of care.

4. Sample Requirements

- Gene panel and direct mutation tests will be initially be performed on FFPE samples obtained at biopsy or surgical resection or from cytology samples.

- **For Pan-Cancer Large NGS Panel** (500+ genes), please send:

- **For samples with >20% neoplastic cells**: two tubes (Eppendorf or Universal), each containing 5 x 10µm sections (curls/scrolls)

- **For samples with <20% neoplastic cells**: 20 x 5µm slide mounted sections along with 1 H&E with regions of >20% neoplastic cells highlighted.

- **For FISH tests**, please send:
  - Samples that are 2 x 4µm and 2 x 2µm sections on 'APES' or 'sticky' slides per test required with an accompanying H&E slide with the appropriate tumour rich area(s) marked.

- **For other Molecular Pathology tests**, please send:
  - **For samples with >30% neoplastic cells:** 5 x 10µm sections (curls/scrolls) in a clean universal.
  - **For samples with <30% neoplastic cells**: 10 x 5µm slide mounted sections along with 1 H&E with regions of >30% neoplastic cells highlighted.

5. Formalin Fixed tissue preparation and processing

In order to preserve viable RNA in tumour samples for analysis of fusion transcripts, it is essential to follow clean procedures.

- Gloves should be worn at all times
- The microtome and forceps must be cleaned before use with lotoxane and then IMS.
- For each new block a **fresh section of blade** should be used and the microtome and forceps wiped with IMS.
- If a water bath is needed this should be **cleaned** thoroughly between cases.

Scrolls/curls

- Blocks should be trimmed of excess wax before the scrolls are cut.
- As per the sample requirements above, scrolls should be cut and placed into an Eppendorf or Universal tube. The greater the number of scrolls (or the bigger the tissue area) the higher the DNA and RNA yield is likely to be. The use of scrolls will not allow macro-dissection of the samples prior to DNA extraction so please ensure that each scroll has >20% neoplastic content.

Slide mounted sections

- As per sample requirements above, sections should be cut and mounted onto slides. The greater the number of sections used (or the bigger the tissue area) the higher the DNA yield is likely to be.
- The use of mounted sections will allow for macro-dissection (scraping with a scalpel) of the neoplastic area (using an accompanying marked H&E slide as a

guide) into a tube, this will help to ensure the material going forward into the DNA extraction has >20% neoplastic content.

6. Sample labelling, the request form and transport

- The SWGLH requires all samples for genetic testing to be appropriately labelled with patient name, date of birth and pathology block number.

- Cancer genetic tests should be requested using the SW GLH cancer request form available at https://www.nbt.nhs.uk/south-west-genomic-laboratory-hub

- In order to avoid delays, it is essential that the information about who the report should be sent to is included on the request form. We recommend an email address, or preferably an email group.

- Samples should be sent urgently to the SWGLH using the dedicated rapid transport service The destination address is:

  Bristol Genetics Laboratory
  Pathology Sciences
  Southmead Hospital
  Southmead
  Bristol
  BS10 5NB

  The sample transport pathways are as follows:

Cheltenham General and Gloucestershire Royal Royal United Hospitals Bath University Hospitals Bristol Weston General	**Pathology inter-site transport service**
University Hospitals Plymouth North Devon District Royal Cornwall Hospitals Royal Devon and Exeter Hospital Musgrove Park Taunton and Yeovil District Torbay and South Devon	**HPV transport service**

7. The turnaround times for genetic tests?

- The SWGLH aims to report gene panel analysis **within 7-10 working days of sample receipt** at the Genetics Laboratory to help ensure that genetic information is available to clinicians to guide selection of treatment for cancer.

- For special circumstances, when genetic test results are required more urgently than this, the SWGLH may provide an urgent service in which a rapid single gene test may be performed instead of the large gene panel. This approach will also be taken in the event of scanty or poor quality material. Clinicians or Pathologists are invited to contact the Bristol Genetic laboratory directly to access this service.

- **To enable rapid turnaround times, it is critical that decisions to request genetic testing, processing and transport of tissue samples to the SW GLH occurs as rapidly as possible after sample collection.**

8. Further information

The main source of information will be the SW GLH website:

https://www.nbt.nhs.uk/south-west-genomic-laboratory-hub

For further information or for feedback, please contact the SW GLH team directly:

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