2022_03

# SCOTTISH MOLECULAR PATHOLOGY LABORATORY CONSORTIUM

## GENOMIC TEST DIRECTORY FOR MOLECULAR PATHOLOGY

NHS SCOTLAND

NHS National Services Scotland

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# INTRODUCTION

## NHS SCOTLAND LABORATORY GENETIC SERVICES

NHS Scotland genetics services are delivered through four regional genetics centres in Aberdeen, Dundee, Edinburgh and Glasgow. Each centre offers a closely integrated laboratory and clinical service. NHS National Services Scotland commission the four genetics centres in Scotland work as a formal consortium arrangement, to deliver equitable, high quality genetic testing service for Scotland. All laboratories are accredited by United Kingdom Accreditation Service (UKAS) in accordance with the recognized ISO 15189:2012 standard.

Molecular genetics testing was nationally designated in 1985 and cytogenetics in 2009. Molecular pathology testing services was nationally commissioned as a single designated multi-site national specialist service from 1 April 2013.

Genetics and molecular pathology services are evolving and increasing each year with advancing knowledge, technology, and the increasing utility of stratified medicine. The increase in molecular pathology, in particular, is increasingly being driven by the development and availability of targeted treatment therapies in both solid tumours and haematological malignancies.

Molecular pathology centres deliver the vast majority of services on a regional basis, providing testing for the local and neighbouring healthboards. A limited number of specialist tests are provided in designated centres to cover the population of Scotland.

## PURPOSE OF DOCUMENT

The Scottish Molecular Pathology Laboratory Consortium Genomic Test Directory contains a list of all services currently available in Scotland.

This document will be reviewed annually.

## NHS SCOTLAND GENETIC LABORATORY CONTACT DETAILS

- **Aberdeen (NHS Grampian)**
  Address: Genetics and Molecular Pathology Laboratory Services, Polwarth Building, Foresterhill, Aberdeen AB25 2ZD
  Email address: gram.molgen@nhs.scot
  Website: https://www.nhsgrampian.org/service-hub/north-of-scotland-medical-genetics

- **Dundee (NHS Tayside)**
  Address: East of Scotland Regional Genetics Service, Level 6, Ninewells Hospital, Dundee DD1 9SY

Email address: Tay.esrg@nhs.scot
Website: https://www.nhstayside.scot.nhs.uk/OurServicesA-Z/Genetics/PROD_295540/index.htm

- **Edinburgh Genetics (NHS Lothian)**
  Address: South East Scotland Genetic Service, Western General Hospital, Crewe Road, Edinburgh, EH4 2XU
  Email address: edinburgh.dna@nhslothian.scot.nhs.uk / wgh.cytogenetics@nhslothian.scot.nhs.uk
  Phone : 0131 537 1116 / 0131 537 1940
  Website:https://services.nhslothian.scot/clinicalgeneticsservice/GeneticLaboratoryServices/Pages/default.aspx

- **Edinburgh Molecular Pathology (NHS Lothian)**
  ***Molecular Pathology – Solid Tumours***, Department of Laboratory Medicine, Royal Infirmary of Edinburgh, 51 Little France Crescent, Old Dalkeith Road, Edinburgh EH16 4SA
  Email address :molecular.pathology@nhslothian.scot.nhs.uk
  Tel: 0131 242 7141
  ***Haematology Malignancy Diagnostic Service (HMDS)***, Haematology/Biochemistry Combined Reception, Department of Laboratory medicine, Western General Hospital, Crewe Road, Edinburgh EH4 2XU
  Email address: HMDS.Lothian@nhslothian.scot.nhs.uk
  Tel: 0131 537 1145/2374

- **Glasgow (NHS Greater Glasgow & Clyde)**
  Address: West of Scotland Centre for Genomic Medicine, Laboratory Genetics, Level 2B Laboratory Medicine & FM Building, Queen Elizabeth University Hospital, Glasgow G51 4TF
  Email address: Genetic.Laboratories@ggc.scot.nhs.uk
  Website: https://www.nhsggc.org.uk/about-us/professional-support-sites/laboratory-medicine/laboratory-disciplines/laboratory-genetics/#

## TEST REQUESTING

Testing will be delivered either in the local centre or the designated centre, according to the test directory. Regardless of testing centre, all samples should be directed to the local genetics laboratory in the first instance, with referrals being forwarded by them where required/if appropriate. Samples should be accompanied with the appropriate completed referral forms (or proforma, if required). For local sample acceptance policies and referral forms, please see the local laboratory website.

Consent for genetic testing should be gained for testing before the sample is referred to the laboratories. This is of particular importance in testing where there may be germline implications and a possible impact on family members e.g. BRCA1/2 testing in ovarian tumours, inherited predisposition to haematological malignancies.

Services are provided for the clinical indications listed when referred from the appropriate specialties.

## SAMPLE REQUIREMENTS

A range of sample types may be referred for molecular pathology testing including blood, marrow, formalin fixed paraffin embedded (FFPE) tissue etc. For specific sample requirements associated with each test, please see the local laboratory websites.

## TESTING METHODOLOGY

Different methods are utilised depending on the scope of testing. These methods include techniques to detect a single variant up to genome wide screens. The different methods include:

- PCR (polymerase chain reaction)
- Sanger sequencing
- Next Generation Sequencing (NGS; DNA or RNA based) panels – vary in size from a small, targeted panels to gene screens and may include detection of fusion genes Fragment analysis
- Multiplex Ligation Probe Amplification (MLPA) including methylation specific type (MS-MLPA)
- Fluorescent In Situ Hybridisation (FISH)
- PCR/FLA (fragment length analysis)
- Pyrosequencing (pyroseq), including MS-pyroseq
- Allele specific PCR (COBAS)
- Karyotype
- Microarray (SNP array)
- qRT PCR (quantitative real-time PCR)
- RT-PCR (reverse transcription PCR)
- Real time AS-PCR (allele specific PCR)
- High resolution melt
- Nested RT-PCR

## SCOPE AND RANGE OF TEST

The scope and range of testing refers to the extent of testing and the types of variant that will be detected.

The scope of testing includes:

- Targeted screen – testing of specific region(s) e.g. gene rearrangements, amplifications or DNA level variant
- Whole gene screen – sequence of coding region of relevant gene(s)
- Copy number (variant)/(CNV) – assessment of gene level copy number
- Genomic screen – detection of large scale rearrangements

The types of variants detected include:

- Small sequence variants
    - Single nucleotide variants (SNVs)
    - Insertions / deletions (indels)
- Copy number variants (CNVs)
    - Exon level
    - Genome wide level
- Genome wide rearrangements

The targets tested refer to the genes / regions tested for the particular clinical indication.

## REPORTING TIMES

Reporting times are listed based on calendar days (except where indicated). These range from 3 to 42 days depending on urgency and complexity of testing. NB. Different reporting times may be evident in some clinical indications due to differences in local clinical practice.

# SOLID MALIGNANCIES

## ADULT GRANULOSA CELL TUMOUR

### AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | Sanger | Targeted screen | SNV | FOXL2 (Cys134Trp) | 14 |
| Dundee | Sanger | Targeted screen | SNV | FOXL2 (Cys134Trp) | 14 |
| EdinburghMP | Sanger | Targeted screen | SNV | FOXL2 (Cys134Trp) | 14 |
| Glasgow | Sanger | Targeted screen | SNV | FOXL2 (Cys134Trp) | 14 |

### REFERRAL CRITERIA

- Ovarian sex cord stromal tumour – differential diagnosis includes adult granulosa cell tumour

### REQUESTING SPECIALTIES

- Pathology
- Gynaecological MDT

# BREAST CANCER

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | FISH | Targeted screen | Copy number | ERBB2 (HER2) | 14 |
| Dundee | FISH | Targeted screen | Copy number | ERBB2 (HER2) | 14 |
| EdinburghMP | FISH | Targeted screen | Copy number | ERBB2 (HER2) | 14 |
| Glasgow | FISH | Targeted screen | Copy number | ERBB2 (HER2) | 14 |

## REFERRAL CRITERIA

- Invasive primary breast cancer, recurrent and metastatic tumours identified to have borderline HER2 expression by immohistochemistry (IHC) (score of 2+)

## REQUESTING SPECIALTIES

- Pathology
- Oncology

# COLORECTAL CANCER

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | NGS_DNA | Targeted screen | SNVs, indels | KRAS (codons 12, 13, 59, 61, 117, 146)<br>NRAS (codons 12, 13, 59, 61, 117, 146)<br>BRAF (codon 600) | 14 |
| | PCR/FLA | Targeted screen | MSI | NR21, NR24, BAT26, BAT25, MONO27 microsatelllite repeats | 14 |
| | MS-MLPA | Targeted screen | methylation | MLH1 | 14 |
| Dundee | NGS_DNA | Targeted screen | SNVs, indels | KRAS (codons 12, 13, 59, 61,117, 146)<br>NRAS (codons 12, 13, 59, 61)<br>BRAF (codon 600) | 14 |
| | PCR/FLA | Targeted screen | MSI | NR21, NR24, BAT26, BAT25, MONO27 microsatelllite repeats | 14 |
| | MS-MLPA | Targeted screen | methylation | MLH1 | 28 |
| EdinburghMP | NGS_DNA | Targeted screen | SNVs, indels | KRAS (codons 12, 13, 59, 61, 117, 146)<br>NRAS (codons 12, 13, 59, 61)<br>BRAF (codon 600)<br>TP53 (if requested by Oncology) | 14 |
| | PCR/FLA | Targeted screen | MSI | NR21, NR24, BAT26, BAT25, MONO27 microsatellite repeats | 14 |
| | MS-pyroseq | Targeted screen | methylation | MLH1 | 28 |
| Glasgow | NGS_DNA | Targeted screen | SNVs, indels | KRAS (codons 12, 13, 59, 61, 117, 146)<br>NRAS (codons 12, 13, 59, 61)<br>BRAF (codon 600) | 14 |
| | PCR/FLA | Targeted screen | MSI | NR21, NR24, BAT26, Bat25, MONO27 microsatellite repeats | 7 |
| | MS-pyroseq | Targeted screen | methylation | MLH1 | 14 |

NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

- All new diagnoses of colorectal cancer

## REQUESTING SPECIALTIES

- Pathology
- Oncology

# GASTRIC CANCER

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | FISH | Targeted screen | Copy number | ERBB2 (HER2) | 14 |
| Dundee | FISH | Targeted screen | Copy number | ERBB2 (HER2)<br>EGFR | 14 |
| EdinburghMP | FISH | Targeted screen | Copy number | ERBB2 (HER2) | 14 |
| Glasgow | FISH | Targeted screen | Copy number | ERBB2 (HER2) | 14 |

## REFERRAL CRITERIA

- Upper GI (gastric and gastro-oesophageal) biopsies or excisions

Reflex FISH testing acceptance criteria:

- Testing is initiated by MDT
- Cases scored as HER2 IHC 0, 1+ or 3+ do not require FISH
- HER2 IHC 2+ require FISH testing

Reflex testing is not done on:

- Negative (0, 1+) HER2 IHC cases
- Positive (+++) HER2 IHC cases
- Patients for surgery who may not need Herceptin/chemotherapy treatment
- Very frail patients who will be given "best supportive care" only

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# GASTROINTESTINAL TUMOURS

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Dundee | NGS_DNA | Targeted screen | SNVs, indels | KIT (exons 9, 11, 13, 17, region of 8)<br>PDGFRA (exons 12, 14, 18)<br>BRAF (codon 600) | 14 |
| EdinburghMP | NGS_DNA | Targeted screen | SNVs, indels | KIT (exons 9, 11, 13, 17)<br>PDGFRA (exons 12, 14, 18)<br>BRAF (codon 600) | 14 |

## REFERRAL CRITERIA

- Analysis of all resected moderate-risk and high-risk GISTs, regardless of location, is recommended, as well as all diagnostic biopsies in which neoadjuvant therapy is contemplated and all biopsies of inoperable GIST.

- In some cases, mutational analysis may be of direct diagnostic value. Identification of a typical mutation seen in GISTs may be of value in supporting the diagnosis of GIST, particularly if a broader differential diagnosis had previously been considered.

- The clinical utility of characterising secondary mutations to guide subsequent oncological management remains uncertain.

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# GLIOMA (INCLUDING HIGH GRADE)

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| EdinburghMP | NGS_DNA | Targeted screen | SNVs, indels | IDH1 (codon 132)<br>IDH2 (codon 172)<br>BRAF (codon 600)<br>TP53 (hotspots) | 14 |
| | MS-pyroseq | Targeted screen | methylation | MGMT | 7 |
| Glasgow | NGS_DNA | Targeted screen | SNVs, indels | IDH1 (codon 132)<br>IDH2 (codon 172)<br>BRAF (codon 600) | 14 |
| | MS-pyroseq | Targeted screen | methylation | MGMT | 7 |

## REFERRAL CRITERIA

- Investigations are performed as directed by referral following neuropathological assessment and diagnosis of glioma

## REQUESTING SPECIALTIES

- Oncology
- Neuropathology

# HEAD AND NECK CANCER (SQUAMOUS)

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Glasgow | PCR/FLA | Targeted screen | Types 16 and 18 | HPV type 16/18 | 14 |

## REFERRAL CRITERIA

- Analysis is performed following pathological assessment in patients undergoing investigations for head & neck squamous cell carcinoma (HNSCC).

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# LUNG CANCER

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | NGS_DNA | Targeted screen | SNVs, indels | EGFR (exons 18, 19, 20, 21)<br>KRAS (codons 12, 13, 61)<br>BRAF (codon 600) | 14 |
| | NGS_RNA | Targeted screen | Specific rearrangements | ALK<br>ROS1<br>RET | 14 |
| | FISH | Targeted screen | Specific rearrangements | ALK<br>ROS1<br>RET | 14 |
| Dundee | NGS_DNA | Targeted screen | SNVs, indels | EGFR (exons 18, 19, 20, 21)<br>KRAS (codons 12, 13, 61)<br>BRAF (codon 600) | 14 |
| EdinburghMP | NGS_DNA | Targeted screen | SNVs, indels | EGFR (exons 18, 19, 20, 21)<br>KRAS (codons 12, 13, 61)<br>BRAF (codon 600)<br>Additional targets: FGFR, MET | 14 |
| | FISH | Targeted screen | Specific rearrangements | ALK<br>ROS1<br>RET (upon request) | 14 |
| Glasgow | NGS_DNA | Targeted screen | SNVs, indels | EGFR (exons 18, 19, 20, 21)<br>KRAS (codons 12, 13, 61)<br>BRAF (codon 600) | 14 |
| | FISH | Targeted screen | Specific rearrangements | ALK<br>ROS1 | 14 |

## REFERRAL CRITERIA

- Usually non-squamous Non Small Cell Lung Cancer (NSCLC) although there may be scenarios where clinicians wish to test other subtypes of NSCLC e.g. never smokers or long-time ex-smokers with squamous tumours, tumours with unusual phenotype, eligible for tyrosine kinase inhibitor therapy.

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# LUNG CANCER, CELL FREE DNA

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | Allele specific PCR (COBAS) | Targeted screen | SNVs, indels | EGFR (exons 18, 19, 20, 21) | 7 |
| EdinburghMP | Allele specific PCR (COBAS) | Targeted screen | SNVs, indels | EGFR (exons 18, 19, 20, 21) | 7 |

## REFERRAL CRITERIA

- Non-squamous Non Small Cell Lung Cancer (NSCLC)/Lung Cancer patients, where
  - no biopsy material is available, or
  - biopsy material is unsuitable for molecular analysis, or
  - patient unwell and biopsy cannot be obtained, or
  - for monitoring purposes to detect emergence of resistance mutations, or
  - patient otherwise eligible for tyrosine kinase inhibitor therapy

## REQUESTING SPECIALTIES

- Oncology

# MELANOMA (MALIGNANT, METASTATIC)

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | NGS_DNA | Targeted screen | SNVs, indels | BRAF (codon 600)<br>NRAS (codons 12, 13, 59, 61)<br>KIT (exon 9, 11, 13, 17) | 14 |
| Dundee | NGS_DNA | Targeted screen | SNVs, indels | BRAF (codon 600)<br>NRAS (codons 12, 13, 59, 61)<br>KIT (exon 9, 11, 13, 17, 18) | 14 |
| EdinburghMP | NGS_DNA | Targeted screen | SNVs, indels | BRAF (codon 600)<br>NRAS (codons 12, 13, 59, 61)<br>KIT (exon 9, 11, 13, 17, 18)<br>GNA11 additional target – reported if present | 14 |
| Glasgow | NGS_DNA | Targeted screen | SNVs, indels | BRAF (codon 600)<br>NRAS (codons 12, 13, 59, 61)<br>KIT (exon 9, 11, 13, 17) | 14 |

## REFERRAL CRITERIA

- Request from Oncology/MDT for patients with metastatic disease, or locally advanced progression, being considered for adjuvant therapy

- If, following review, the patient's co-morbidities exclude them from adjuvant therapy testing is not indicated

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# MESOTHELIOMA

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | FISH | Targeted screen | Copy number | CDKN2A/CEP9 | 21 |
| Dundee | FISH | Targeted screen | Copy number | CDKN2A/CEP9 | 14 |
| Glasgow | FISH | Targeted screen | Copy number | CDKN2A/CEP9 | 14 |

NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

- Diagnostic uncertainty re: mesothelioma or benign or reactive mesothelial proliferation

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# MUCOEPIDERMOID CARCINOMA

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Dundee | FISH | Targeted screen | Specific rearrangements | MAML2 | 14 |

## REFERRAL CRITERIA

- Salivary gland excision specimens/core biopsies
  - To confirm morphological impression of a mucoepidermoid carcinoma (MEC) in challenging/higher grade cases
  - To exclude a MEC when it is among a list of differentials in a hard to classify tumour (such as a tumour comprising predominantly of clear cells or oncocytic cells)
  - In a core biopsy of a salivary tumour where diagnosis is challenging and extensive surgery is planned

- Jaw cysts
  - Where mucous cells are prominent to exclude intraosseous MEC

- Lymph node
  - Where tumour deposits look like metastatic MEC (primary site may be unknown)

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# NEUROBLASTOMA

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | FISH | Targeted screen | Copy number | MYCN | 3 |
| | FISH | Targeted screen | Copy number | 1p, 11q and 17 status | 14 |
| EdinburghG | FISH | Targeted screen | Copy number | MYCN | 3 |
| | SNP array | Genomic screen | Copy number | MYCN, 1p, 11q and 17 status | 14 |
| Glasgow | FISH | Targeted screen | Copy number | MYCN | 3 |

## REFERRAL CRITERIA

- Investigations are performed as directed by referral following neuropathological assessment and diagnosis of neuroblastoma

## REQUESTING SPECIALTIES

- Oncology
- Neuropathology

# OLIGODENDROGLIOMA

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Glasgow | FISH | Targeted screen | Copy number | 1p/19q (PET specimens) | 14 |
| EdinburghG | FISH | Targeted screen | Copy number | 1p/19q (PET specimens) | 14 |
| | SNP array | Genomic screen | Copy number | 1p/19q status<br>whole genome (fresh/frozen tissue) | 14 |

## REFERRAL CRITERIA

- Investigations are performed as directed by referral following neuropathological assessment and diagnosis of oligodendroglioma

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# OVARIAN CANCER

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | NGS_DNA | Whole gene screen | SNVs, indels | BRCA1 and BRCA2 | 42 |
| Glasgow | NGS_DNA | Whole gene screen | SNVs, indels | BRCA1 and BRCA2 | 42 |

## REFERRAL CRITERIA

- First line/maintenance - newly diagnosed, advanced (FIGO stage III or stage IV), high grade epithelial ovarian cancer, fallopian tube or primary peritoneal cancer that is in response (complete or partial) to platinum based chemotherapy

- Second line/relapsed - platinum-sensitive relapsed high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete response or partial response) to platinum based chemotherapy

**N.B**. Germline testing of *BRCA1* and *BRCA2* is also available in these patients, and should be performed in parallel. Please refer to the Scottish Genetics Laboratory Consortium Genomic Test Directory for Rare & Inherited Disease

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# RENAL CELL CARCINOMA (RCC)

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | FISH | Targeted screen | Specific rearrangements | Depending on type;<br>$TFE_3$<br>$VHL/CEP_3$ | 21 |
| | Microarray | Genomic screen | Copy number | Whole chromosome or whole chromosome arm gains / losses | 21 |
| Dundee | FISH | Targeted screen | Specific rearrangements | $TFE_3$ | 21 |
| | NGS_DNA Sanger/MLPA | Whole gene screen and CNV | SNVs, indels, exon level CNV | VHL<br>SDH<br>FH<br>FLCN | 56 |
| EdinburghMP | FISH | Targeted screen | Specific rearrangements | $TFE_3$<br>VHL<br>ALK | 14 |

NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

Testing should be considered in the following cases when the results will impact diagnosis and patient management:-

- A younger age group of less than 30 years (and may be considered for the 30 to 40 year age group)
- A strong family history of renal tumours
- Multiple tumours (in the absence of a known genetic syndrome)
- A rare tumour type with genetic associations
- For the above points germline testing (NGS_DNA/Sanger/MLPA) would be recommended first.
- SDH and FH testing of tumour following on from suggestive IHC but no germline pathogenic variant detected
- Unusual morphology
- $TFE_3$ testing can be used to make a diagnosis of a MiT translocation tumour which may also be important for treatment
- Copy number variant analysis of chromosome 3p aids diagnosis of clear cell renal carcinoma
- Copy number variant analysis can help distinguish between oncocytoma, chromophobe RCC and papillary RCC
- ALK associated RCC can occur in children with sickle cell trait or adults without sickle cell trait (rare)

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# SARCOMA

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | FISH | Targeted screen | Gene rearrangements and amplifications | EWSR1, SS18, FOXO1, FUS, MDM2, USP6 | 21 (EWSR1 – 7) |
| Dundee | FISH | Targeted screen | Specific rearrangements | EWSR1, SS18, COL1A1::PDGFB | 14 |
| EdinburghMP | FISH | Targeted screen | Gene rearrangements and amplifications | DDIT3, COL1A1, EWSR1, FOXO1, FUS, JAZF1, MDM2, SS18, TFE3, USP6 | 14 |
| | NGS_DNA | Targeted screen | SNVs, indels | GNAS, CTNNB1 | 14 |
| Glasgow | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 28 |
| | FISH | Targeted screen | Gene rearrangements and amplifications | *SS18, EWSR1, FOXO1, PAX7::FOXO1, PAX3::FOXO1, FUS, DDIT3* and *MDM2* | 14 |
| | PCR/FLA | Targeted screen | Specific rearrangements | *SS18::SSX1, SS18::SSX2, EWSR1::FLI1, PAX3::FOXO1, PAX7::FOXO1*, and *FUS::CREB3L2* | 14 |

## REFERRAL CRITERIA

- Translocation sarcoma where differential diagnosis includes such tumours [Ewing's sarcoma / round cell tumours, alveolar rhabdomyosarcoma, myxoid liposarcoma, synovial sarcoma, low grade fibromyxoid sarcoma/sclerosing epithelioid fibrosarcoma, alveolar soft part sarcoma, clear cell sarcomas, endometrial stromal sarcoma, Dermatofibrosarcoma protuberans (DFSP)].
- MDM2 gene amplification for tumours where differential diagnosis includes atypical lipomatous tumour, well differentiated liposarcoma, dedifferentiated liposarcoma, parosteal osteosarcoma, low grade central osteosarcoma.
- CTNNB1 mutation testing to help clinical management for cases where differential diagnosis includes desmoid fibromatosis
- GNAS mutation for fibrous dysplasia.
- USP6 rearrangement for cases where diagnostic clarification is required [myofibroblastic/fibroblastic lesions such as nodular fasciitis and bone lesions such as aneurysmal bone cysts or mimics]

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# SOLID TUMOUR, OTHER

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | FISH | Targeted screen | Specific rearrangements | As indicated/required | 21 |
| | Karyotype | Genomic screen | Large scale rearrangements | As indicated/required | 21 |
| Dundee | FISH | Targeted screen | Specific rearrangements | As indicated/required | 21 |
| | Karyotype | Genomic screen | Large scale rearrangements | As indicated/required | 21 |
| EdinburghG | FISH | Targeted screen | Specific rearrangements | As indicated/required | 21 |
| | SNP array | Genomic screen | Specific rearrangements | As indicated/required | 21 |
| Glasgow | FISH | Targeted screen | Specific rearrangements | As indicated/required | 21 |
| | Karyotype | Genomic screen | Large scale rearrangements | As indicated/required | 21 |

## REFERRAL CRITERIA

- A tumour biopsy where available genetic testing would aid in the diagnosis or prognostication

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# THYROID CANCER

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | NGS_DNA | Targeted screen | SNV, indels | BRAF (codon 600)<br>HRAS (codon 12, 13, 61)<br>KRAS (codon 12, 13, 61, 117, 146)<br>NRAS (codon 12, 13, 59, 61)<br>RET mutation (hotspot) | 14 |
| | FISH or NGS_RNA | Targeted screen | Specific rearrangements | RET | 14 |
| Dundee | NGS_DNA or pyroseq | Targeted screen | SNV, indels | BRAF (codon 600)<br>KRAS (codon 12, 13, 61, 117, 146)<br>NRAS (codon 12, 13, 59, 61)<br>RET mutation (hotspot) | 14 |
| EdinburghMP | NGS_DNA | Targeted screen | SNV, indels | BRAF (codon 600)<br>HRAS (codon 12, 13, 61)<br>KRAS (codon 12, 13, 61, 117, 146)<br>NRAS (codon 12, 13, 59, 61)<br>RET mutation (hotspot)<br>TP53 (hotspots) | 14 |
| | FISH | Targeted screen | Specific rearrangements | RET | 14 |
| Glasgow | NGS_DNA | Targeted screen | SNV, indels | BRAF (codon 600)<br>HRAS (codon 12, 13, 61)<br>KRAS (codon 12, 13, 61, 117, 146)<br>NRAS (codon 12, 13, 59, 61)<br>RET mutation (hotspot) | 14 |

## REFERRAL CRITERIA

- BRAF and/or RAS mutations for indeterminate nodules and malignant tumours
- RET fusions for papillary/anaplastic carcinoma
- RET mutations for medullary/anaplastic carcinoma

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# UVEAL MELANOMA

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| EdinburghMP | NGS_DNA | Targeted screen | SNV, indels | GNA11, GNAQ (hotspots) | 14 |
| Glasgow | NGS_DNA | Targeted screen | SNV, indels | BRAF (codon 600) | 14 |
| | FISH | Targeted screen | Specific CNV | Chromosomes 3, 6, 8 | 14 |

## REFERRAL CRITERIA

- Primary uveal melanoma

## REQUESTING SPECIALTIES

- Oncology
- Pathology

# HAEMATOLOGICAL MALIGNANCIES

## ACUTE LYMPHOBLASTIC LEUKAEMIA (ALL)

### AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | Karyotype | Genomic screen | Large scale rearrangements | All<br>(within resolution of method) | 14 |
| | FISH | Targeted screen | Specific rearrangements | B-ALL:<br>BCR::ABL1<br>ETV6::RUNX1<br>TCF3::PBX1<br>TCF3::HLF<br>FIP1L1::PDGFRA<br>KMT2A<br>PDGFRB<br>ABL1 and 2<br>Others if required e.g. ploidy<br><br>T-ALL:<br>ABL1<br>ABL2<br>FIP1L1::PDGFRA<br>PDGFRB | 14<br>(BCR::ABL- 3) |
| | Array | Genomic screen | Genomic screen<br>Ploidy and (specific) deletions | *EBF1*, *IKZF1*, *CDKN2A/B*, *PAX5*, *ETV6*, *BTG1*, *RB1* and *PAR1* (CRLF2) | 14 |
| | NGS_RNA | Targeted screen | Specific rearrangements | Including:<br>BCR::ABL1 (qualitative)<br>ETV6::RUNX1<br>TCF3::PBX1<br>TCF3::HLF<br>KMT2A::AFF1<br>KMT2A::MLLT1<br>KMT2A::MLLT3<br>KMT2A::MLLT4<br>KMT2A::MLLT10<br>KMT2A::ELL | 14 |
| Dundee | Karyotype | Genomic screen | Large scale rearrangements | All<br>(within resolution of method) | 21<br>(if urgent - 14) |
| | FISH | Targeted screen | Specific rearrangements | BCR::ABL1<br>ETV6::RUNX1<br>KMT2A (MLL)<br>Ploidy<br><br>If required screening for ABL-class gene fusions<br>ABL1,ABL2,<br>PDGRFA and<br>PDGRFB::CSF1R,<br>FIP1L1::PDGFRA<br>T-CELL TCRA/D | 14<br>(BCR-ABL- 3) |

| | | | | | |
|---|---|---|---|---|---|
| | Array | Genomic screen (if requested by clinician) | Genomic screen Ploidy and (specific) deletions | EBF1, IKZF1, CDKN2A/B, PAX5, ETV6, BTG1, RB1 and PAR1 (CRFL2), iAMP21 | 14 |
| EdinburghG | Karyotype | Genomic screen | Large scale rearrangements | All<br>(within resolution of method) | 14 |
| | FISH | Targeted screen | Specific rearrangements | B-cell:<br>BCR::ABL1,<br>ETV6::RUNX1,<br>TCF3::-PBX1<br>TCF3::HLF<br>KMT2A<br>ploidy.<br><br>If required screening for ABL-class fusions:-<br>ABL1, ABL2,<br>FIP1L1::PDGRFA<br>PDGRFB<br><br>T-cell:<br>TCRAD, TCRB.<br>If required screening for ABL-class fusions:-<br>ABL1, ABL2,<br>FIP1L1::PDGRFA<br>PDGRFB | 7 |
| | Array | SNP Array | Genomic screen Ploidy and (specific) deletions | *EBF1*, *IKZF1*, *CDKN2A/B*, *PAX5*, *ETV6*, *BTG1*, *RB1* and *PAR1* (CRLF2) | 14 |
| EdinburghMP | RT-PCR | Targeted screen | Specific rearrangements | BCR::ABL1<br>ETV6::RUNX1<br>TCF3::PBX1<br>KMT2A::AFF1<br>KMT2A::MLLT1<br>KMT2A::MLLT3<br>KMT2A::AFDN<br>KMT2A::ELL | 3* |
| Glasgow | Karyotype | Genomic screen | Large scale rearrangements | All<br>(within resolution of method) | 14 |
| | Array | Genomic screen | Genomic screen Ploidy and (specific) deletions | BTG1, CDKN2A/b, EBF1, ETV6, IKZF1, PAX5, PAR1 (CRLF2) and RB1<br>Ploidy group determination<br>iAMP21 | 14 |
| | FISH | Targeted screen | Specific rearrangements | B-cell:<br>*BCR::ABL1*,<br>*ETV6::RUNX*<br>*TCF3::PBX1*<br>*TCF3::HLF*<br>*KMT2A*<br>ploidy.<br><br>If required screening for ABL-class fusions:-<br>*ABL1, ABL2,*<br>*FIP1L1:: PDGRFA*<br>*PDGRFB* | 7<br>(if urgent - 3) |

| | | | | | |
|---|---|---|---|---|---|
| | | | | T-cell:<br>Screening for ABL-class fusions:-<br>*ABL1, ABL2*<br>*FIP1L1::PDGRFA*<br>*PDGRFB* | |
| | PCR/FLA | Targeted screen | Specific rearrangements | BCR::ABL (qualitative) | 14<br>(if urgent - 7) |

* refers to working days
NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

- New diagnosis of acute lymphoblastic leukaemia (ALL)
- Relapsed ALL

## REQUESTING SPECIALTIES

- Haematology

# ACUTE LYMPHOBLASTIC LEUKAEMIA (ALL), MINIMAL RESIDUAL DISEASE (MRD)

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | qRT-PCR | Targeted screen | Specific rearrangements | BCR::ABL1 quantitation [E1A2 and E13A2/E14A2] | 21 |
| Dundee | qRT-PCR (GeneXpert) | Targeted screen | Specific rearrangements | BCR::ABL1 quantitation [E1A2 and E13A2/E14A2] | 14 |
| Edinburgh MP | RT-PCR | Targeted screen | Specific rearrangements | BCR::ABL1 quantitation [E1A2 and E13A2/E14A2]<br>ETV6::RUNX1 (relative)<br>TCF3::PBX1 (relative) | 14 |
| Glasgow | qRT-PCR | Targeted screen | Specific rearrangements | BCR::ABL1 quantitation [E1A2 and E13A2/E14A2] | 14 |
| | Seq/qPCR | Targeted screen | Specific rearrangements | IgH/TCR gene rearrangement work up | 28 |
| | qPCR | Targeted screen | Specific rearrangements | MRD patient specific monitoring (day 29 and week 14) | 7 |

NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

- BCR-ABL1
  - All patients with a BCR-ABL1 rearrangement identified at diagnosis
  - Patients on tyrosine kinase inhibitor therapy (treatment response assessment)
  - Patients undergoing reduced intensity conditioning (RIC) allograft for BCR-ABL1 positive ALL require BCR-ABL monitoring every 3 months post-transplant for a minimum of 2 years.
- IgH/TCR minimal residual disease
  - Paediatric and young adult patients (≤45 years) with a new diagnosis of ALL should be referred for MRD target identification (IgH/TCR gene rearrangements) and follow up as per trial protocols (ALLTogether trial)
  - 'Off-trial' MRD analysis and monitoring is available for paediatric and young adult patients who are not enrolled on the trial
  - Older adults requiring MRD are referred on a case-by-case basis by the managing team and samples are sent to the adult reference laboratory in London

## REQUESTING SPECIALTIES

- Haematology

# ACUTE MYELOID LEUKAEMIA (AML)

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | Karyotype | Genomic screen | Large scale rearrangements | All<br>(within resolution of method) | 14 |
| | NGS_RNA | Targeted screen | Specific rearrangements | Including:<br>BCR::ABL1 (qualitative)<br>RUNX1::RUNX1T1<br>CBFB::MYH11<br>PML::RARA (qualitative)<br>KMT2A::AFF1<br>KMT2A::MLLT1<br>KMT2A::MLLT3<br>KMT2A::MLLT4<br>KMT2A::MLLT10<br>KMT2A::ELL | 14 |
| | PCR/FLA | Targeted screen | Specific rearrangements | FLT3 ITD & TKD, NPM1 | 14<br>(FLT3- 7) |
| | FISH | Targeted screen | Specific rearrangements | As required/indicated :<br>BCR::ABL1<br>RUNX1::RUNX1T1<br>PML::RARA<br>DEK::NUP214<br>KMT2A<br>CBFB<br>MECOM<br>Chr 5 and 7 (copy number) | 14<br>(PML::RARA - 3) |
| | NGS_DNA | Targeted screen | SNV, indels | Myeloid NGS Panel (agreed whole gene / hot-spots | 28 |
| Dundee | Karyotype | Genomic screen | Large scale rearrangements | All<br>(within resolution of method) | 14 |
| | Array | Genomic screen<br>(Used if karyotype poor quality) | Large scale and targeted rearrangements | All<br>(within resolution of method) | 14 |
| | FISH | Targeted screen | Specific rearrangements | As required/indicated<br>BCR::ABL1<br>RUNX1::RUNX1T1,<br>CBFB::MYH11<br>PML::RARA<br>KMT2A<br>MECOM | 14<br>(PML::RARA or BCR::ABL1 - 3) |
| EdinburghG | Karyotype | Genomic screen | Large scale rearrangements | All<br>(within resolution of method) | 14 |
| | FISH | Targeted screen | Specific rearrangements | KMT2A<br>EVI1<br>and others as required/indicated<br>FAST FISH: MDS5, MDS7 and 3q26 | 14<br>(3 if urgent) |
| EdinburghMP | RT-PCR | Targeted screen | Specific rearrangements | BCR::ABL1<br>RUNX1::RUNX1T1<br>CBFB::MYH11 | 3* |

| | | | | | |
|---|---|---|---|---|---|
| | | | | PML::RARA<br>KMT2A::AFF1<br>KMT2A::AFDN<br>KMT2A::MLLT1<br>KMT2A::MLLT3<br>KMT2A::ELL | |
| | PCR/FLA | Targeted screen | Specific rearrangements | FLT3 ITD & TKD<br>NPM1 | 3* |
| | NGS_DNA | Targeted screen | Specific rearrangements | CBF Leukaemia only: KIT (exons 9, 11, 13, 17) | 14 |
| | NGS_DNA | Targeted screen | SNVs, indels | Myeloid NGS panel Panel (agreed whole gene / hot-spots) | 42 |
| | NGS_RNA | Targeted screen | Multiple rearrangements | Myeloid NGS panel Panel | 42 |
| Glasgow | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 14 |
| | RT-PCR | Targeted screen | Specific rearrangements | BCR::ABL (quantitative and qualitative),<br>RUNX1::RUNX1T1<br>CBFB::MYH11 inv (16)<br>PML::RARA (qualitative)<br>FLT3 ITD & TKD, NPM1 | 14 |
| | Sanger | Targeted screen | Specific rearrangements | FLT3 (codon 835, 836) | 14 |
| | FISH | Targeted screen | Specific rearrangements | As required/indicated e.g.<br>*BCR::ABL1*<br>*RUNX1::RUNX1T1*<br>*PML::RARA*<br>*DEK::NUP214*<br>*KMT2A*<br>*MECOM*<br>*CBFB*<br>Chr 5 and 7 (loss/deletion)<br>*TP53*/17 centromere | 3<br>(same day PML-RARA if received before 1pm) |

*refers to working days
NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

Morphologically or immunophenotypically identified acute myeloid leukaemia or likely AML

- Intensive-treatment eligible AML :
- Not fit for intensive treatment: FLT3 NPM1 G-banding and MLL MECOM/3q26 FISH as appropriate
- Relapse – in accordance with clinical requirements and diagnostic findings.

Myeloid NGS panel - All intensive treatment-eligible AML patients (<65). Selected relapsed AML patients to provide therapeutic information.

## REQUESTING SPECIALTIES

- Haematology

# ACUTE MYELOID LEUKAEMIA (AML)
# REMISSION STATUS ASSESSMENT (MINIMAL RESIDUAL DISEASE, MRD)

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | qRT-PCR | Targeted screen | Specific rearrangement | BCR::ABL1 quantitation | 21 |
| Dundee | qRT-PCR (GeneXpert) | Targeted screen | Specific rearrangement | BCR::ABL1 quantitation | 14 |
| Edinburgh MP | RT-PCR | Targeted screen | Specific rearrangements | BCR::ABL1 [quantitative]<br>RUNX1::RUNX1T1 [quantitative]<br>PML::RARA [quantitative]<br>CBFB::MYH11 [quantitative] | 14 |
| | RT-PCR | Targeted screen | Specific rearrangements | NPM1 (type A, B, D) [quantitative] | 7<br>(3* post cycle 2) |
| Glasgow | qRT-PCR | Targeted screen | Specific rearrangements | BCR::ABL1 quantitation | 14 |

*refers to working days
NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

First assessment

- Molecular analysis : PML::RARA, CBFB::MYH11, RUNX1::RUNX1T1, BCR::ABL1 fusion or NPM1 mutation (type A, B, D)
- Other abnormalities (e.g. KMT2A; uncommon NPM1 mutation – by arrangement/send away)

Subsequent assessments

- Molecular analysis : PML::RARA, CBFB::MYH11, RUNX1::RUNX1T1, BCR::ABL1 fusion or NPM1 mutation (type A, B, D)
- Other abnormalities (e.g. KMT2A; uncommon NPM1 mutation – by arrangement/send away)

Note – NGS is not routinely used for monitoring of remission status.

## REQUESTING SPECIALTIES

- Haematology

# CHIMAERISM

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | Targets | TAT |
|---|---|---|---|---|
| Glasgow | PCR/FLA | STR pre-transplant assessment | Screening performed for 11 EuroChimerism STR markers | 30 |
| | | Whole blood post-transplant chimerism<br>Lineage-specific post-transplant chimerism | Informative markers as selected during pre-transplant assessment | 14 |
| | FISH | X/Y sex markers | X and Y chromosome | 7 |

## REFERRAL CRITERIA

- All patients and potential donors being considered for allogeneic stem cell transplant for any indication should be referred for STR pre-transplant assessment
- Whole blood post-transplant chimerism is performed at day 14-28 and then from Day 50 as required
- Lineage-specific post-transplant chimerism monitoring is performed for adult patients from Day 50 and for paediatric patients by request

## REQUESTING SPECIALTIES

- Haematology

# CHRONIC LYMPHOCYTIC LEUKAEMIA (CLL)

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | FISH | Targeted screen | Specific rearrangements | TP53<br>IGH::CCND1 if requested | 21 |
| | NGS_DNA | Whole gene screen | SNVs, indels | TP53 | 21 |
| Dundee | Array | Genomic screen | Large scale and targeted rearrangements | TP53, ATM, 13q14, trisomy 12. Any other relevant findings including CNN LOH | 21 |
| | Sanger | Whole gene screen | SNVs, indels | TP53 | 21 |
| EdinburghG | FISH | Targeted screen | Specific rearrangements | TP53, ATM<br>IGH::CCND1 if requested | 21 |
| EdinburghMP | Sanger | Whole gene screen | SNVs, indels | TP53<br>IGHV mutation status | 21 |
| Glasgow | FISH | Targeted screen | Specific rearrangements | TP53, ATM<br>Differential diagnoses: TP53, ATM and *IGH::CCND1*, 13q14, 13q34, and 12 centromere | 21 |
| | Sanger | Whole gene screen | SNVs, indels | TP53 | 28 |

NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

- Prior to treatment – Assessment of TP53 status (even if previously performed)
- IGH/CCND1 undertaken to aid in differential diagnoses

## REQUESTING SPECIALTIES

- Haematology

# CHRONIC MYELOID LEUKAEMIA (CML)

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 14 |
| | FISH | Targeted screen | Specific rearrangements | BCR::ABL1 | 3 |
| | NGS_RNA | Targeted screen | Specific rearrangements | BCR::ABL1 (qualitative) | 14 |
| Dundee | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 14 (if urgent - 10) |
| | FISH | Targeted screen | Specific rearrangements | BCR::ABL1 | 3 |
| | qRT-PCR (GeneXpert) | Targeted screen | Specific rearrangements | BCR::ABL1 (qualitative) | 14 |
| EdinburghG | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 14 |
| | FISH | Targeted screen | Specific rearrangements | BCR::ABL1 | 3 |
| EdinburghMP | RT-PCR | Targeted screen | Specific rearrangements | BCR::ABL1 (qualitative and quantitative) | 3 |
| Glasgow | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | FISH | Targeted screen | Specific rearrangements | *BCR::ABL1* | 7 (if urgent - 3) |
| | RT-PCR | Targeted screen | Specific rearrangements | *BCR::ABL1* (qualitative and quantitative) | 14 (if urgent - 7) |

NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

- Chronic Myeloid Leukaemia (CML) or suspected Chronic Myeloid Leukaemia. Molecular assessment will aid diagnosis or management (identify fusion variant for MRD).

## REQUESTING SPECIALTIES

- Haematology

# CHRONIC MYELOID LEUKAEMIA (CML), MINIMAL RESIDUAL DISEASE (MRD)

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | qRT-PCR | Targeted screen | Specific rearrangement | BCR::ABL1 quantitation [E1A2 and E13A2/E14A2] | 21 |
| | Sanger | Targeted screen | SNVs, indels | BCR::ABL1 kinase domain mutation (KDM) | 21 |
| Dundee | qRT-PCR (GeneXpert) | Targeted screen | Specific rearrangement | BCR::ABL1 quantitation [E1A2 and E13A2/E14A2] | 14 |
| EdinburghMP | qRT-PCR | Targeted screen | Specific rearrangement | BCR::ABL1 quantitation [E1A2 and E13A2/E14A2] | 14 |
| | Sanger | Targeted screen | SNVs, indels | BCR::ABL1 kinase domain mutation (KDM) | 21 |
| Glasgow | qRT-PCR | Targeted screen | Specific rearrangement | *BCR::ABL1* quantitation [E1A2 and E13A2/E14A2] | 14 |

NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

- MRD assessment to aid management.
- Clinically thought to have BCR-ABL1 TKD resistance mutations.

## REQUESTING SPECIALTIES

- Haematology

# LEUKAEMIA, OTHER

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | FISH | Targeted screen | Specific rearrangements | As indicated/required | 7 |
| | NGS_RNA | Targeted screen | Specific rearrangements | As indicated/required | 14 |
| Dundee | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | FISH | Targeted screen | Specific rearrangements | As indicated/required | 7 |
| EdinburghG | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | FISH | Targeted screen | Specific rearrangements | As indicated/required | 7 |
| Glasgow | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | FISH | Targeted screen | Specific rearrangements | As indicated/required | 7 |

## REFERRAL CRITERIA

- Suspected acute leukaemia with clinical reasons to suspect translocation, or indication of likely translocation on karyotyping. Assessment will aid diagnosis or management.

## REQUESTING SPECIALTIES

- Haematology

## LYMPHOMA/LYMPHOPROLIFERATIVE DISEASE

### AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | FISH | Targeted screen | Specific rearrangements | DLBCL: MYC with BCL2 and BCL6 where required. | 21 (Burkitt-7) |
| | | | | Burkitt lymphoma: MYC with BCL2 and BCL6 where required. | |
| | | | | Burkitt-like lymphoma (if MYC negative) : 11q23/q24/cen | |
| | | | | Follicular lymphoma: BCL2 | |
| | | | | Mantle cell lymphoma : IGH::CCND1 | |
| | | | | Anaplastic large cell lymphoma (ALCL) : ALK, DUSP22::IRF4 | |
| | | | | MALT lymphoma: MALT1 | |
| | PCR/FLA | Targeted screen | Clonality studies | IgH, IgK PCR assay<br>TCRG, TCRB PCR assay | 21 |
| | RT-PCR | Targeted screen | Specific variant | MYD88 (p.L265P) as requested | 21 |
| | Sanger | Targeted screen | Specific variant | Hairy cell leukaemia: BRAF (p.V600E) | 21 |
| Dundee | FISH | Targeted screen | Specific rearrangements | High Grade B cell MYC, IGH::MYC with BCL2 and BCL6 where required. | 21 High grade/Burkitt MYC - 14 |
| | | | | Burkitt: MYC, IGH::MYC with BCL2 and BCL6 where required. | |
| | | | | Follicular lymphoma: BCL2, IGH::BCL2 | |
| | | | | Mantle cell lymphoma: CCND1, IGH::CCND1 | |
| | | | | Anaplastic large cell lymphoma: ALK, DUSP22::IRF4 | |
| | | | | MALT: MALT1, IGH::MALT1, with BIRC3::MALT1, BCL6 if required | |
| | | | | DLBCL: MYC, BCL2, BCL6, IGH::MYC, IGH::BCL2, IRF4::DUSP22 where required | |
| | PCR/FLA | Targeted screen | Clonality studies | IgH, IgK PCR assay<br>TCRG, TCRB PCR assay | 21 |
| EdinburghG | FISH | Targeted screen | Specific rearrangements | High-grade B Cell lymphoma : MYC - with BCL2, BCL6, IGH-MYC, IGH, IGK, IGL where required | 14 |
| | | | | Burkitt-like lymphoma (if MYC negative) : 11q23/q24/cen | |
| | | | | Follicular lymphoma : BCL2 (and BCL6 if requested) | |
| | | | | Mantle cell lymphoma : IGH-CCND1 | |
| | | | | ALCL: ALK (if negative then DUSP22/IRF4 and/or TP63 on request) | |
| | | | | MALT lymphoma : MALT1 | |
| EdinburghMP | PCR/FLA | Targeted screen | Clonality studies | IGH IGK IGL clonality<br>TCRB TCRG clonality [TCRD if appropriate] | 14 |
| | Real time AS-PCR | Targeted screen | Specific variant | MYD88 (p.L265P) | 14 |
| | Pyroseq | Targeted screen | Specific variant | Hairy cell leukaemia: BRAF (p.V600E) | 14 |

| | | | | | |
|---|---|---|---|---|---|
| Glasgow | Karyotype (if fresh material available) | Genomic screen | Large scale rearrangements | All<br>(within resolution of method) | 28 |
| | FISH | Targeted screen | Specific rearrangements | High grade lymphoma: MYC, *IGH::MYC*.<br>If MYC rearranged, *IGH::BCL2* and *BCL6* | 14<br>(MYC-3)<br><br>14 for NHL<br>(if urgent - 3) |
| | | | | Follicular lymphoma: *IGH::BCL2*.<br>If *BCL2* not rearranged, *BCL6* | |
| | | | | Mantle cell lymphoma IGH::CCND1 | |
| | | | | ALCL: ALK, DUSP22/IRF4 | |
| | | | | MALT lymphoma : MALT1.<br>If MALT rearranged, *BIRC3::MALT1* | |
| | | | | T-PLL: TCL1 | |
| | PCR/FLA | Targeted screen | Clonality studies | IgH, IgK PCR assay<br>TCRG, TCRB PCR assay | 21 |
| | Sanger | Targeted screen | Specific variant | MYD88 (p.L265P) | 14 |

NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

- Investigations to aid diagnosis and classification of lymphoma / lymphoproliferative disorder.
  - G-banding [where bone marrow involvement has been confirmed]
  - IG and TCR clonality where required
  - Appropriate FISH and molecular assay depending on suspected disease sub type [see table]

## REQUESTING SPECIALTIES

- Haematology

# MYELOMA

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | FISH | Targeted screen | Specific rearrangements | IGH::FGFR3<br>IGH::MAFB<br>IGH::PDGFRA<br>TP53<br>CDKN2C<br>CKS1B | 21 |
| Dundee | FISH | Targeted screen | Specific rearrangements | IGH::FGFR3<br>IGH::MAF<br>IGH::MAFB<br>CKS1B::CDKN2C<br>D13S319::13q34<br>TP53 | 21 |
| EdinburghG | FISH | Targeted screen | Specific rearrangements | IGH::FGFR3<br>IGH::MAF<br>TP53<br>CKS1B::CDKN2C | 21 |
| Glasgow | FISH | Targeted screen | Specific rearrangements | *IGH::FGFR3*<br>*IGH::MAF*<br>IGH BAR<br>*TP53*<br>*CDKN2C and CKS1B*<br>*ATM*<br>*IGH::CCND1* | 21 |

## REFERRAL CRITERIA

- Transplant eligible only: FISH analysis on CD138+ plasma cells
- Patients with poor response to initial therapy (WoSCAN CMG guidelines)
- Patients in whom the treating clinician thinks it will alter therapy (WoSCAN CMG guidelines)

## REQUESTING SPECIALTIES

- Haematology

# MYELOPROLIFERATIVE NEOPLASMS (MPN)

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | FISH | Targeted screen | Specific rearrangements | FIPL1::PDGFRA<br>PDGFRB | 21 |
| | NGS_RNA | Targeted screen | Specific rearrangements | FIPL1::PDGFRA<br>PDGFRB<br>FGFR1 | 21 |
| | PCR/FLA | Targeted screen | Specific variants; SNVs, indels as indicated | Differential diagnoses:<br>JAK2 p.(V617F)<br>JAK2 (exon 12)<br>CALR exon 9 insertions and deletions<br>MPL p.(W515L) | 21 |
| | qRT-PCR | Targeted screen | SNV | KIT D816V | 21 |
| | NGS_DNA | Targeted screen | SNV, indels | Myeloid NGS Panel (agreed whole gene / hot-spots | 42 |
| Dundee | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21<br>(10 if urgent) |
| | Array | Genomic screen (Used if karyotype poor quality) | Large scale and targeted rearrangements | All (within resolution of method) | 21 |
| | FISH | Targeted screen | Specific rearrangements | FIPL1::PDGFRA<br>PDGFRB | 21 |
| | PCR/FLA and Sanger | Targeted screen | Specific variants; SNVs, indels | MPD: JAK2 p.(V617F)<br>JAK2 (exon12)<br>CALR exon 9 insertions and deletions<br>MPL exon 10<br>KIT D816V | 21 |
| EdinburghG | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | FISH | Targeted screen | Specific rearrangements | BCR::ABL1 (if requested)<br>Eosinophilia and Hypereosinophilia:<br>FIPL1::PDGFRA<br>PDGFRB<br>FGFR1 | 21 |
| EdinburghMP | RT AS-PCR | Targeted screen | Specific variants | KIT D816V | 14 |
| | RT AS-PCR | Targeted screen | Specific variants | JAK2 (V617F) | 21 |
| | High resolution melt analysis | Targeted screen | Specific variants; SNVs, indels | JAK2 exon 12 mutation<br>MPL exon 10 p.(W515 and S505) | 28 |
| | PCR/FLA | Targeted screen | Specific variants; SNVs, indels | CALR exon 9 mutation | 28 |
| | Nested RT-PCR | Targeted screen | Specific rearrangements | FIP1L1::PDGFRA | 14 |

| | | | | | |
|---|---|---|---|---|---|
| Glasgow | Karyotype | Genomic screen | Large scale rearrangements | All<br>(within resolution of method) | 21 |
| | FISH | Targeted screen | Specific rearrangements | *BCR::ABL* if requested<br>*FIP1L1::PDGFRA*<br>*PDGFRB*<br>*FGFR1*<br>20q deletion | 7<br>(3 if urgent) |
| | PCR/FLA | Targeted screen | Specific variants; SNVs, indels | JAK2 p.(V617F)<br>JAK2 (exon12)<br>CALR exon 9 insertions and deletions<br>MPL exon 10 p.(W515L) | 21 |

NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

- Myeloproliferative neoplasm (MPN) or suspected Myeloproliferative Neoplasm. Molecular assessment will aid diagnosis or management.
- For extended Myeloid NGS panel: Atypical MPNs (triple negative PMF phenotype, MDS/MPN overlap). Molecular assessment will aid diagnosis or management.

## REQUESTING SPECIALTIES

- Haematology

# MYELODYSPLASTIC SYNDROME

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | FISH | Targeted screen | Specific rearrangements | monosomy 5/5q-<br>monosomy 7/7q-<br>TP53 (on 5q- syndrome)<br>others as required | 21 |
| | NGS_DNA | Whole gene screen | SNVs, indels | TP53 (5q- syndrome) | 21 |
| | NGS_DNA | Targeted screen | SNV, indels | Myeloid NGS Panel<br>(agreed whole gene / hot-spots | 42 |
| Dundee | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | Array | Genomic screen (Used if karyotype poor quality) | Large scale and targeted rearrangements | All (within resolution of method) | 21 |
| | FISH | Targeted screen | Specific rearrangements | monosomy 5/5q-<br>monosomy 7/7q-<br>TP53 (on 5q- syndrome)<br>others as required | 21 |
| | Sanger | Whole gene screen | SNVs, indels | TP53 (5q- syndrome) | 21 |
| EdinburghG | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | FISH | Targeted screen | Specific rearrangements | High risk MDS patients:<br>monosomy 5/5q-<br>monosomy 7/7q-<br>EVI1 (3q26)<br>TP53 (on 5q- syndrome) | 21<br>(3 – HR MDS) |
| EdinburghMP | NGS_DNA | Targeted screen | SNVs, indels | Myeloid NGS panel Panel<br>(agreed whole gene / hot-spots) | 42 |
| | NGS_RNA | Targeted screen | Multiple rearrangements | Myeloid NGS panel Panel<br>(agreed fusion panel) | 42 |
| Glasgow | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | FISH | Targeted screen | Specific rearrangements | monosomy 5/5q-<br>monosomy 7/7q-<br>TP53 (on 5q- syndrome)<br>20q , and others as required | 3 |
| | Sanger | Whole gene screen | SNVs, indels | TP53 (5q- syndrome) | 28 |

NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

- Known or suspected / high risk for the development of myelodysplasia. Assessment will aid diagnosis or management.
- Myeloid NGS panel: All transplant-eligible MDS patients (both low- and high-risk patient cohorts)(<65) / For differentiation of hypoplastic MDS/aplastic anaemia.

## REQUESTING SPECIALTIES

- Haemataology

# PRIMARY MYELOFIBROSIS (UNDER 70YEARS)

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | PCR/FLA | Targeted screen | Specific variants; SNVs, indels | MPD: JAK2 V617F<br>CALR exon 9<br>MPL exon 10 p.(W515L) | 21 |
| | NGS_DNA | Targeted screen | SNV, indels | Myeloid NGS Panel (agreed whole gene / hot-spots | 28 |
| Dundee | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | PCR/FLA / Sanger | Targeted screen | Specific variants; SNVs, indels | MPD: JAK2 V617F<br>CALR exon 9<br>MPL exon 10 | 21 |
| EdinburghG | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| EdinburghMP | Real time AS-PCR | Targeted screen | Specific variants; SNV, indels | JAK2 (V617F) | 21 |
| | High resolution melt analysis | Targeted screen | Specific variants; SNVs, indels | CALR exon 9<br>MPL exon 10 p.(W515 and S505) | 28 |
| | PCR/FLA | Targeted screen | Specific variants; SNVs, indels | CALR exon 9 | 28 |
| | NGS_DNA | Targeted screen | SNV, indels | Myeloid NGS Panel (agreed whole gene / hot-spots | 42 |
| | NGS_RNA | Targeted screen | Multiple rearrangements | Myeloid NGS Panel | 42 |
| Glasgow | Karyotype | Genomic screen | Large scale rearrangements | All (within resolution of method) | 21 |
| | PCR/FLA | Targeted screen | Specific variants; SNVs, indels | MPD: JAK2 V617F<br>CALR exon 9<br>MPL exon 10 p.(W515) | 21 |

NB Reporting times influenced by local clinical practice

## REFERRAL CRITERIA

- Primary Myelofibrosis (PMF) or suspected PMF. Assessment will aid diagnosis or management.
- Myeloid NGS panel: All transplant-eligible patients with PMF (<65)

## REQUESTING SPECIALTIES

- Haematology

# PHARMACOGENOMIC TESTING

## DIHYDROPYRIMIDINE DEHYDROGENASE DEFICIENCY (DPYD)

### AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Aberdeen | Sanger | Targeted screen | Specific SNVs | *c.1236G>A/HapB3<br>c.1679T>G<br>c.1905+1G>A<br>c.2846A>T | 14 |
| Dundee | Sanger | Targeted screen | Specific SNVs | *c.1236G>/HapB3<br>c.1679T>G<br>c.1905+1G>A<br>c.2846A>T | 14 |
| EdinburghMP | PCR/FLA | Targeted screen | Specific SNVs | *c.1236G>/HapB3<br>c.1679T>G<br>c.1905+1G>A<br>c.2846A>T | 14 |
| Glasgow | PCR/FLA | Targeted screen | Specific SNVs | *c.1236G>/HapB3<br>c.1679T>G<br>c.1905+1G>A<br>c.2846A>T | 14 |

*c.1236G>A may be reported as c.1129-5923C>G (HapB3 – in linkage disequilibrium)

### REFERRAL CRITERIA

- Patients potentially receiving fluoropyrimidine treatment

### REQUESTING SPECIALTIES

- Oncology

# THIOPURINE S-METHYLTRANSFERASE (TPMT) DEFICIENCY

## AVAILABLE TESTING

| Centre | Method | Scope and range of test | | Targets | TAT |
|---|---|---|---|---|---|
| Glasgow | PCR/FLA | Targeted screen | Specific SNVs | c.238G>C<br>c.460G>A<br>c.719A>G | 14 |

## REFERRAL CRITERIA

- Patients potentially receiving thiopurine treatment.
- Patients with chronic inflammatory and autoimmune conditions, leukaemia and who may be subject to post-transplant rejection.

## REQUESTING SPECIALTIES

- Oncology