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A partnership between Newcastle University and Newcastle Hospitals NHS Foundation Trust

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## Clinical Services Information for Users

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Details of all services are also available at [www.newgene.org.uk](http://www.newgene.org.uk) or email: [info@newgene.org.uk](mailto:info@newgene.org.uk)

NewGene Ltd uses high through put genotyping, DNA sequencing and real time PCR to provide clinical laboratory services, principally to haematology, pathology and clinical genetics departments.

**Laboratory opening hours:** The laboratory is staffed between 8.30am and 5.00pm Monday to Friday.

NewGene is accredited with the United Kingdom Accreditation Service (UKAS) to ISO standard 15189 (medical laboratories). Where tests are marked \* below, these are recently introduced to the test repertoire and lie outside the current scope of accreditation.

Clinical scientists are registered with the Health and Care Professions Council.

The laboratory participates in the following external quality assurance schemes:

- GenQA (Genomic Quality Assessment) European Molecular Quality Network (EMQN)
- UK NEQAS for Leucocyte Immunophenotyping

For tests where no formal EQA scheme exists, an informal method of proficiency testing is in place.

### List of tests and sample requirements

Alport syndrome\* - full gene sequencing using next generation sequencing technology

Whole blood samples in 4.5ml EDTA tubes or 4µg of DNA (260/280 1.8-2.0).

Genes included in the assay are *COL4A3*, *COL4A4*, *COL4A5*.

BCR-ABL fusion gene targeted mutation analysis

Whole blood samples in 4.5ml EDTA tubes, to arrive within 48 hours of the sample being taken.

BCR-ABL monitoring in chronic myeloid leukaemia

This test requires RNA and therefore whole blood samples should be collected and arrive at the NewGene laboratory within 48 hours of the sample being taken.

BRAF targeted mutation detection (colorectal cancer, melanoma, hairy cell leukaemia)

Whole blood samples in 4.5ml EDTA tubes for hairy cell leukaemia.

Formalin fixed paraffin embedded (FFPE) samples in the form of tumour blocks, cut curls (minimum of 4 x 6µm thick curls) or cytology slides. Ideally tumour content should be 30% of the specimen.

BRCA1 and BRCA2 full gene sequencing in hereditary breast cancer using next generation sequencing technology

Whole blood samples in 4.5ml EDTA tubes *or* extracted DNA (2µg total quantity at >50ng/µl).

Copy number analysis using MLPA is performed by the Northern Genetics Service, Newcastle Hospitals NHS Foundation Trust.

cKIT targeted mutation analysis (D816V mutation in mastocytosis\* and acute myeloid leukaemia, exons 8 and 17)

Whole blood samples or bone marrow in 4.5ml EDTA tubes. Mast cell enrichment is recommended for samples referred for mastocytosis testing.

Note – see below for *ckIT* mutation analysis in GIST.

#### *ckIT* and *PDGFRA* mutation analysis in gastrointestinal stromal tumours (GIST)

Formalin fixed paraffin embedded (FFPE) samples in the form of tumour blocks, cut curls (minimum of 4 x 6µm thick curls) or cytology slides. Ideally tumour content should be 30% of the specimen.

#### *EGFR* and *KRAS* targeted mutation detection (non-small-cell lung cancer)

Formalin fixed paraffin embedded (FFPE) samples in the form of tumour blocks, cut curls (minimum of 4 x 6µm thick curls), cytology slides or fixed cell suspensions. Ideally tumour should be histologically classified as adenocarcinoma and tumour content should be 30% of the specimen.

#### Familial hypercholesterolemia

Whole blood samples in 4.5ml EDTA tubes. Targeted mutation detection of 20 selected mutations in *LDLR*, *APOB* and *PCSK9*. Also, detection of 12 SNPs in various key genes that allow calculation of a 'SNP-score' which further refines the likelihood of polygenic or monogenic disease.

Samples that are negative in the mutation detection test and where clinically indicated by the regional lipid clinic MDT, will be fully sequenced using next generation sequencing technology, for the genes *LDLR*, *AOE*, *PCSK9* and selected regions of *APOB*.

#### Familial adenomatous polyposis (FAP)\*

Whole blood samples in 4.5ml EDTA tubes or 4µg of DNA (260/280 1.8-2.0). Full gene sequencing using next generation sequencing technology of the coding regions of the *APC* and *MUTYH* genes. Copy number analysis using MLPA is referred to the Northern Genetics Service, Newcastle Hospitals NHS Foundation Trust.

#### Hereditary non-polyposis colorectal cancer\*

Whole blood samples in 4.5ml EDTA tubes or 4µg of DNA (260/280 1.8-2.0). Full gene sequencing using next generation sequencing technology, of the coding regions of four genes: *MLH1*, *MSH2*, *MSH6* (excluding exon 1) and *PMS2*, and sequencing of the 3' untranslated region of *EPCAM*. Copy number analysis using MLPA is referred to the Northern Genetics Service, Newcastle Hospitals NHS Foundation Trust.

#### *JAK2* V617F mutation, *JAK2* exon 12 mutations and *MPL* and Calreticulin (*CALR*) targeted mutation detection in myeloproliferative neoplasms

Whole blood samples in 4.5ml EDTA tubes

#### *KRAS* and *NRAS* targeted mutation detection in colorectal tumours

Formalin fixed paraffin embedded (FFPE) samples in the form of tumour blocks, cut curls (minimum of 5 curls) or cytology slides. Ideally tumour content should be 30% of the specimen.

#### Marfan syndrome\*

Whole blood samples in 4.5ml EDTA tubes or 4µg of DNA (260/280 1.8-2.0). Full gene sequencing using next generation sequencing technology, of the coding region of the *FBN1* gene.

#### Medulloblastoma subgroup classification\* (results issued on a research basis only)

This test examines the methylation signature of DNA extracted from medulloblastoma and determines a subgroup classification (*MB<sub>WNT</sub>*, *MB<sub>SHH</sub>*, *MB<sub>Grp3</sub>* or *MB<sub>Grp4</sub>*) using the web app, MIMIC\* v3.3.4 (Minimal Methylation Classifier). MIMIC has not been validated for clinical use and is for research use only.

Formalin fixed paraffin embedded (FFPE) samples in the form of tumour blocks or cut curls (minimum of 5 curls), or fresh tissue samples. Ideally tumour content should be >50% of the specimen.

Samples must have a confirmed histopathological diagnosis of medulloblastoma.

### TPMT genotyping

Whole blood samples in 4.5ml EDTA tubes

### TP53 full gene sequencing

Whole blood samples in 4.5ml EDTA tubes *or* extracted DNA (1µg total quantity at >50ng/µl).

\*Indicates test is NOT in scope of accreditation

## Referral procedure

1. All sample tubes must be labelled with the following minimum information:
  - Full name of the patient
  - Date of birth of the patient
2. Pathology blocks must be labelled with the histopathology block reference of the referring laboratory.
3. All samples should be accompanied by a request form. These are available as downloads from the NewGene web site or on request (0191 242 1923).

If it is not possible to use a referral form, the required information should be provided in a letter.

The information provided on the form must include:

- Full name of the patient
- Date of birth
- Sex of the patient
- NHS number
- Patient's postcode
- Tests required
- Name of referring clinician, address for issue of report and contact telephone number

### **Samples which do not conform to these criteria may be discarded.**

Ensure that the name and date of birth on the card are exactly the same as those on the sample tube.

Special care should be taken to ensure that forenames and surnames are clearly distinguished.

## Sample transport

Specific referral instructions for the different tests are given on the relevant referral forms. Samples should be delivered as follows -

By post, courier, taxi or hospital delivery van as soon as possible after the sample is taken to

- NewGene Ltd
- Institute of Genetic Medicine
- Biomedicine East Wing
- International Centre for Life
- Central Parkway
- Newcastle upon Tyne
- NE1 3BZ

Note: Referrals for myeloproliferative neoplasm tests (JAK2, MPN and calreticulin) should be sent to the Protein Laboratory, Haematology Dept., Leazes Wing, Royal Victoria Infirmary, Newcastle upon Tyne.

## Sample packaging

Samples should be properly packaged by the referrer. Packaging should be strong and of good quality. In addition to the sample receptacle, there should be two further layers of packaging that should be closed and sealed to prevent any loss of contents. There should be sufficient cushioning to prevent breakage of the primary receptacle. The outer layer of packaging should be rigid. Please contact the laboratory (0191 242 1923) with any queries, and see:

<http://www.hse.gov.uk/aboutus/meetings/committees/acdp/050208/acdp88p6.pdf> .

Note: Special delivery bags are available on request for KRAS referrals only

High risk samples should be clearly labelled in an appropriate manner (see below).

## Hazardous samples

Samples known or suspected to be a biological hazard **must** be identified as such by the use of appropriate hazard warning labels. Please contact the laboratory before referring samples from patients where a prion-related disorder is suspected.

## Consent for testing and data storage

Consent for DNA testing must be obtained from the patient by the referring clinician prior to referral of the sample. This is not the responsibility of the NewGene laboratory staff.

Personal data is stored by the laboratory but is only used for analytical and reporting purposes associated with the required test.

## Referral laboratories

The vast majority of the tests in the NewGene repertoire are performed in the NewGene laboratory.

The exceptions are:

- (1) Copy number analysis of BRCA1 and BRCA2 which forms an important part of the BRCA full gene sequencing test, is performed by the Northern Genetics Service, Newcastle Hospitals NHS Foundation Trust, using MLPA analysis, when required.
- (2) Samples that require Sanger sequencing are PCR amplified at NewGene, but then transferred to the Northern Genetics Service, Newcastle Hospitals NHS Foundation Trust, which is UKAS accredited to ISO15189 (reference 9028) for the Sequencing reactions to be carried out. Following capillary analysis, raw data is returned to NewGene.

The sequencing data is analysed by NewGene staff prior to reporting.

## Contacts

### Laboratory address:

NewGene Ltd  
Institute of Genetic Medicine  
Biomedicine East Wing  
International Centre for Life  
Newcastle upon Tyne  
NE1 3BZ  
United Kingdom

### CEO:

Dr Angela Silmon (0191 242 1923) [angela.silmon@newgene.org.uk](mailto:angela.silmon@newgene.org.uk)

### Laboratory Manager:

Jane Lisgo (0191 242 1923) [jane.lisgo@nuth.nhs.uk](mailto:jane.lisgo@nuth.nhs.uk)

### Clinical Scientists:

Dr Louise Johnston (0191 242 1923) [louise.johnston@nuth.nhs.uk](mailto:louise.johnston@nuth.nhs.uk)

## Advice concerning samples, test results and assay performance

Advice is available from registered Clinical Scientists, Dr Louise Johnston, (Louise.Johnston@nuth.nhs.uk), Dr Ann Curtis (ann.curtist@nuth.nhs.uk and Dr Laura Ions (Laura.Ions@nuth.nhs.uk),

Where appropriate, information about the sensitivity, specificity and performance of assays is provided in the clinical report along with any factors that may influence the interpretation of results. However. The following general points should be noted:

*Timeliness of receipt of samples* – samples for BCR-ABL monitoring or BCR-ABL fusion gene mutation analysis must arrive at the laboratory within 48 hours of the sample being taken in order that high quality RNA can be obtained. Other samples, where the analyte is DNA, are stable at 4°C for up to 5 days.

*Tumour content* - FFPE samples should ideally contain at least 30% tumour material. It is important that the estimated tumour content is supplied with the referral form.

*Test sensitivity* - For all molecular pathology and molecular haemato-oncology tests, the sensitivity of mutation detection is 5% on a wild type background.

*Next generation sequencing tests* – A minimal coverage of 50-fold is guaranteed for key genes in all gene panel tests. Regions of reduced coverage for key genes will be filled in using Sanger sequencing. Specific details are available on request.

Tests that generate a quantitative result are reviewed with respect to the uncertainty of measurement associated with the numeric value. Specific test information is available on request.

## Comments and complaints

We aim to deliver consistently high standards of care. We are always pleased to hear of anything you have to say and any suggestions you might have to help us continuously improve our services. If you have complaints about our service these will be dealt with promptly according to our customer complaints procedure. Please contact us by telephone, e-mail or letter. Contact details are at the beginning of this information sheet.

## Further information:

Visit the web site: [www.newgene.org.uk](http://www.newgene.org.uk) or email: [info@newgene.org.uk](mailto:info@newgene.org.uk)  
Telephone: 0191 242 1923