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General Information

The Centre was the first haemoglobinopathy prenatal diagnosis centre to be established in the UK (1975). At that time prenatal diagnosis was performed by fetal blood sampling and biochemical techniques using globin chain biosynthesis studies. The molecular diagnostic laboratory was established in 1992 after developing the obstetric technique of chorionic villus sampling with obstetric colleagues at UCLH and collaborating with other molecular research laboratories to develop the molecular methods.

The molecular genetics laboratory is a National Centre for the diagnosis of the haemoglobin disorders. In addition the laboratory provides an international service for prenatal diagnosis and genotyping for haemoglobin disorders. The molecular Genetics laboratory is a designated specialised DNA laboratory by the NHS Sickle Cell and Thalassaemia Screening Programme and is a member of the UK Genetic Testing Network (UKGTN).

The centre sits within in the directorate of Women’s Health for the clinical service and the Molecular DNA laboratory service is in a joint partnership with UCLH and Health Service Laboratories. The laboratory staff works closely with clinical colleagues and other health care scientists across several directorates and research staff. The staff work in conjunction with the Fetal Medicine Unit at UCLH to provide a prenatal diagnosis and risk assessment service and with the Centre for Reproductive and Genetic Health (CRGH) to provide a collaborative Preimplantation Genetic Diagnosis Service. The laboratory receives samples from clinics of the Trust and particularly the Sickle Cell and Thalassaemia paediatric and adult clinics and also referrers from outside the Trust.

General information on the clinical diagnostic service is described here, however for specific queries please contact the department.

Location

Please address samples to:
University College Hospital NHS Trust
Haemoglobinopathy Genetics
Specimen Reception
The Halo Building
Flaxman Terrace
London WC1H 9AZ

The UCLH specimen reception is located at 60 Whitfield St London W1T 4EU. Samples are sent from the main hospital to Specimen Reception via the ‘Pod’ system and sample deliveries made by courier or from other sites are made via a rear building entrance in Howland Mews. Near Patient Testing facilities for Haematology/Oncology patients are located on the Lower Ground Floor of the MacMillan Cancer Centre on Huntley Street. Services are also located in the main tower and the antenatal clinic in the EGA.
Contact Numbers and Working Hours
Telephone: Direct line 0203447 9458, Fax: 0203447 9864.
Laboratory opening times: Monday- Friday 9.00am to 5.00pm excluding bank holidays

Clinical Service:
Haemoglobinopathy Genetic Clinic, Women’s Health provides:
Specialist haemoglobinopathy genetic counselling
Risk Assessments
Prenatal diagnosis
Consultations for Preimplantation Genetic Diagnosis

For appointments: Contact the Office Manager/PA, Direct line: 0203447 9458, Fax: 0203447 9864. Email uclh.haemoglobinopathygenetics@nhs.net

Or address as below:

Haemoglobinopathy genetics clinics are held on Tuesday AM, although urgent patients may be seen on other days. Clinics are held at:

University College Hospital NHS Foundation Trust
Elizabeth Garrett Anderson Hospital and Obstetric Hospital
Fetal Medicine Unit (second floor)
235 Euston Road
London NW1 2BU

<table>
<thead>
<tr>
<th>Haemoglobinopathy Genetics (Molecular Laboratory)</th>
<th>0203 447 9458 or x79458</th>
<th>9.00 – 17.00 Monday – Friday</th>
</tr>
</thead>
</table>

Scientific and Clinical Departmental Lead: Dr Mary Petrou

Operational matters please contact the operational manager at HSL:
Andrew Levett
Operations Manager Genetics and Molecular Pathology
Levels – 5 & 6 Genetics and Molecular Pathology
TDL Genetics and Health Services Laboratories
The Halo Building, 1 Mabledon Place, London, WC1H 9AX    Main Tel +44 (0) 20 7307 7409 Ext: 3501

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**Urgent Requests**

Please contact the laboratory during routine working hours.

**Out-of-Hours Service (after hours Monday - Saturday, Sunday and Public Holidays).**

There is currently no out of hours service

**Clinical Staff**

**Haemoglobinopathy Consultants**

**Red Cell Joint Unit**

Professor John B Porter  Tel: +44 (0) 20 3447 7359  .: p.a email : maryam.dar@nhs.net

Dr Sara Trompeter  Tel: +44 (0) 20 3447 7359  .: p.a email : maryam.dar@nhs.net

Dr Perla Eleftheriou  Tel: +44 (0) 20 3447 7359  .: p.a email : maryam.dar@nhs.net

Dr Emma Draser  Tel: +44 (0) 20 3447 7359  .: p.a email : maryam.dar@nhs.net

**Haemoglobinopathy Genetics**

Dr Mary Petrou  Tel: +44 (0)20 3447 9458 or Ext 79458  Fax: 020 3447 9864  Email: mary.petrou@nhs.net

Email PA/Office Manager: uclh.haemoglobinopathygenetics@nhs.net

**Clinical advice**

During routine working hours (Monday – Friday 9.00 – 17.00), please contact Dr M Petrou. Out of hours contact the on call haematology consultant via the UCLH switchboard.

**Phlebotomy Services**

For phlebotomy opening times please refer to INSIGHT phlebotomy page via the following link:

http://www.uclh.nhs.uk/OurServices/ServiceA-Z/PATH/PHEB/Pages/Home.aspx
**Making a complaint to the Laboratory**

If you would like to make a complaint relating to a specific test please contact the Laboratory Operational Manager

Alternatively, please complete the online Datix incident reporting procedure available on the intranet and we will investigate your complaint.

**Vacutainer™ Guide**

<table>
<thead>
<tr>
<th>Becton Dickinson Vacutainer™</th>
<th>Ordering Information</th>
<th>Tests / Screens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EDTA 10mls blood</td>
<td>. Haemoglobinopathy Genetics (DNA), Haemocromatosis</td>
</tr>
<tr>
<td>Sterile container, Containing culture medium</td>
<td>Chorionic villus tissue</td>
<td>Prenatal Diagnosis for Haemoglobinopathies</td>
</tr>
<tr>
<td>Sterile container</td>
<td>10mls Amniotic Fluid (another 10mls should be sent to a Cytogenetics lab for back up cultures)</td>
<td>Prenatal Diagnosis for Haemoglobinopathies</td>
</tr>
<tr>
<td></td>
<td>EDTA 2-3mls Fetal blood</td>
<td>Prenatal Diagnosis for Haemoglobinopathies</td>
</tr>
<tr>
<td></td>
<td>EDTA 2mls capillary blood sample</td>
<td>Genotyping for Haemoglobinopathies</td>
</tr>
</tbody>
</table>

**Completion of the request form**

Please use the appropriate request form for the tests required and ballpoint (indelible) ink pen to complete the request form. There are two request forms. Prenatal Diagnosis request form and Genotyping request form. [CLICK HERE](#). UCLH referrers may use electronic ordering for Haemoglobinopathy Genetics. See also the relevant pages on insight.

- Please provide the patient’s full name, hospital number and date of birth.
- Please provide the date and time of sample collection and relevant clinical information to facilitate sample processing and the interpretation of results.
- Please ensure that the destination of the report, the name of the requesting/responsible individual and a contact telephone number for the responsible health professional is provided to enable laboratory staff to notify the responsible health professional regarding unsuitable (urgent) samples and to relay and/or discuss urgent and abnormal results.
Please provide clinical details.

Please ensure that adequate samples are taken for the tests requested and that each sample is labelled correctly. Contact the laboratory for clarification of sample requirements if required.

For all **genotype requests** from outside UCLH please provide haematology results including a full blood count, HPLC/ electrophoresis results and ferritin results if available.

For **fetal samples**, tissue type and date of biopsy should be clearly documented on the request form. In case of twins special attention must be given to the identity of each sample. Send:

- 10mls EDTA blood should be sent from each partner.
- The hematologic results to include a full blood count and HPLC/haemoglobin electrophoresis must also be sent, confirming the haemoglobinopathy carrier states of each partner. If the male partner is not available and has not had a haemoglobinopathy screen and the woman has opted for prenatal diagnosis, then please provide the ethnic origin of the male partner to enable the laboratory to provide a risk assessment.
- Evidence of patient consent by providing a signature on the request form or a copy of your local request form

### Sample Collection (phlebotomy)

The sample collection policy for staff trained in phlebotomy [Haem-PD-BloodSampColl] and guidelines for sample labelling are available on the UCLH Intranet and can be sent electronically to GP practices.

### Sample Labelling

- Please label samples clearly with hospital number, first and last name and date of birth using a ballpoint (permanent/indelible) ink pen. The NHS number may be used in place of the hospital number for GP and non-UCLH Trust patients.
- A minimum of three points of identification must be provided for all samples.

**NOTE:** Samples received broken/leaking, inadequately labelled, aged, clotted, haemolysed or otherwise unsuitable for testing may not be processed. If the requested tests are urgent, laboratory staff will notify the requesting health professional.

### Sample Transport to the Laboratory

UCLH samples: refer to the Pathology Specimen Transport and Pneumatic Tube System policies on the UCLH Intranet for hospital transport. Prenatal Diagnosis samples must not be sent by the Pneumatic Tube System. Samples from GP practices must be sent via UCLH Trust transport; via the next available collection during the working day. Samples from other hospitals should be sent by first class post or courier. Prenatal Diagnosis samples should be sent by courier. Please notify the lab if you are sending prenatal diagnosis samples.
Special Handling Requirements

Please see the ‘Notes’ section in the test tables below, or contact the relevant laboratory for information regarding special handling requirements.

Reporting Results:

For UCLH requests currently reports are scanned onto CDR under documents/Dr Petrou. External referrers reports are sent by confidential email or fax as requested.

Molecular Testing:

The Haemoglobinopathy Molecular Genetics Laboratory provides a comprehensive testing service for all haemoglobinopathy mutations available. All samples are first characterised by a full blood count, HPLC/capillary electrophoresis and then identified by DNA analysis. Mutations tested are shown on the Globin gene server [http://globin.cse.psu.edu/hbvar/menu.html](http://globin.cse.psu.edu/hbvar/menu.html) Refer to [http://2000.apogi.info/](http://2000.apogi.info/) for patient information materials. The following tests are included:

The following are the categories of haemoglobinopathy molecular genetic testing carried out:

**Alpha thalassaemia mutations including alpha+ and alpha0 types**

- These are requested when haematological investigations show microcytic, hypochromic indices and a normal HbA2 level by haemoglobin electrophoresis or HPLC
- DNA diagnosis is the only method to confirm the carrier status of alpha zero thalassaemia trait. When both partners are carriers, the couple is at risk for producing a child with a Haemoglobin Barts Hydrops Fetalis and prenatal diagnosis is indicated. Alpha zero thalassaemia is found in people who originate from the Mediterranean, South East Asia, Far East and Middle East. These forms of Alpha thalassaemia can be detected easily by molecular methods
- Alpha thalassaemia should also be investigated in couples who both carry beta thalassaemia, or one partner carry’s beta thalassaemia and the other partner carry’s a possible alpha-zero thalassaemia and originate from a geographical area where there is a high risk for alpha thalassaemia
- Alpha zero thalassaemia is occasionally found in people originating from India, Pakistan and Africa. If you suspect alpha zero thalassaemia from the haematological parameters contact the department for advice
- Alpha plus thalassaemia trait can only be confirmed by molecular analysis. It is found in people originating from Mediterranean, South East Asia, Far East, Middle East, South Asia, India, Pakistan and Africa
- If both partners carry alpha plus thalassaemia trait, they are not at risk of producing a child with a major Haemoglobinopathy.
**Beta thalassaemia mutations**

Including point mutations and deletions, δβ-thalassaemia, γδβ-thalassaemia, εγδβ-thalassaemia, fusion Hb Lepore thalassaemia and Hb Kenya and the various HPFH disorders

- Beta thalassaemia is also investigated in cases of possible normal/borderline HbA2 beta thalassaemia trait; the red blood cell indices also show a degree of microcytosis. The mutations Cap+1 (A>C), IVS 1-6 (T>C), Poly A (A>G) and Poly A (T>C) often have such borderline results and have been found in the UK populations.

**Sickle Cell Disorders**

The most common include, HbSS, HbSC, HbSD-Punjab, HbSOArab, HbSβ-thalassaemia, HbSHFH.

**Haemoglobin Variants**

Both alpha and beta gene variants. These are requested when routine hematological investigations do not identify the haemoglobin variant.

**Patients with Thalassaemia Major/Intermedia and Sickle Cell Disorders**

- Genotype/phenotype correlation, to aid the clinical management of the patient. Analysis includes beta and alpha globin gene analysis, Xmn polymorphism analysis in the Gγ gene and other gamma mutations. The presence of a mild beta globin mutation, and/or coincidental alpha thalassaemia, and/or the presence of the Xmn polymorphism may be genetic modifiers for reduced disease severity.

**Prenatal Diagnosis**

- β–thalassaemias major/intermedia, β-thalassaemia co-inherited with δβ-thalassaemia, Hb Lepore, HbE, HbO-Arab
- Sickle cell disorders: HbSS, HbSC, HbSβ-thalassaemia, HBSD-Punjab, HbSO-Arab
- Alpha zero thalassaemia (Hb Barts Hydrops Fetalis)
- Severe HbH Disorders and HbH hydrops fetalis involving non-deletion alpha-plus thalassaemia mutations
- Dominant haemoglobin variants

Prenatal Diagnosis investigations involve molecular determination of the fetal genotype and the identification or confirmation of the parental genotypes. According to the best practice guidelines and to provide the most accurate result a minimum of two diagnostic techniques are performed to arrive at the fetal result. The prenatal diagnosis investigation also includes a check for maternal DNA contamination of the fetal sample by the study of the inheritance pattern of polymorphic STR markers from the mother and father.
Table of Genetic Risks the main genetic risks for couples with a haemoglobinopathy that can result in an affected pregnancy are summarised in the table below) (Courtesy if Prof B Modell)
## Testing Information

The following table details the Specimen type; the molecular tests used and turnaround times.

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<th>Carrier of:</th>
<th>α+ thal</th>
<th>α thal type?</th>
<th>α° thal</th>
<th>β thal</th>
<th>δβ thal</th>
<th>Lepore thal</th>
<th>Hb E</th>
<th>Hb O Arab</th>
<th>Hb C</th>
<th>Hb D type</th>
<th>Hb D Punjab</th>
<th>Hb D not Punjab</th>
<th>HPFH</th>
<th>Not a carrier</th>
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**Genetic Risk of Combination**

- **No risk**
- **Serious risk**
- **Less serious risk**
- **Possible hidden risk**
- **Risk in 2nd generation**
- **No info possible**
<table>
<thead>
<tr>
<th>Test</th>
<th>Specimen Type</th>
<th>Reference ranges</th>
<th>Key Factors affecting tests</th>
<th>Notes</th>
<th>Out of hours service</th>
<th>Time Limit for requesting additional tests from time of venesection</th>
<th>Turnaround time from receipt of sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha Thalassaemia</td>
<td>10mls EDTA</td>
<td>Not applicable</td>
<td>Delay in receiving sample</td>
<td>Detection of alpha zero and alpha plus deletions and triplicated/duplicated alpha genes, using Gap-PCR and MLPA. Detection of alpha+ mutations by alpha globin gene sequencing and Restriction enzyme PCR. Send sample ASAP to the laboratory as prolonged storage affects DNA extraction</td>
<td>No service provided</td>
<td>Any time providing sufficient DNA is available</td>
<td>Urgent: 3-10 days</td>
</tr>
<tr>
<td>Beta Thalassaemia</td>
<td>10mls EDTA</td>
<td>Not applicable</td>
<td>Delay in receiving sample</td>
<td>Detection of all point mutations and deletions using ARMS-PCR, Restriction enzyme –PCR, Site Specific Mutagenesis, Gap-PCR, MLPA, DNA sequencing. Send sample ASAP to the laboratory as prolonged storage affects DNA extraction</td>
<td>No service provided</td>
<td>Any time providing sufficient DNA is available</td>
<td>Urgent: 3-10 days</td>
</tr>
<tr>
<td>HPFH and δβ-thalassaemia</td>
<td>10mls EDTA</td>
<td>Not applicable</td>
<td>Delay in receiving sample</td>
<td>Detection of deletions by Gap-PCR and MLPA. Send sample ASAP to the laboratory as prolonged storage affects DNA extraction</td>
<td>No service provided</td>
<td>Any time providing sufficient DNA is available</td>
<td>Urgent: 3-10 days</td>
</tr>
<tr>
<td>Condition</td>
<td>Sample Type</td>
<td>Sample Collection</td>
<td>Sample Storage</td>
<td>Detection Methods</td>
<td>Urgency</td>
<td>Non-Urgency</td>
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<tr>
<td>Sickle Cell</td>
<td>10mls EDTA</td>
<td>Not applicable</td>
<td>Delay in receiving sample</td>
<td>Detection of mutations by ARMS-PCR, Restriction Enzyme PCR, MLPA, DNA sequencing. Send sample ASAP to the laboratory as prolonged storage affects DNA extraction</td>
<td>No service provided</td>
<td>Any time providing sufficient DNA is available</td>
<td>Urgent: 3-10 days</td>
</tr>
<tr>
<td>Haemoglobin Variants (alpha and beta gene variants)</td>
<td>10mls EDTA</td>
<td>Not applicable</td>
<td>Delay in receiving sample</td>
<td>Detection of mutations by ARMS-PCR or HBB, HBA1 and HBA2 sequencing. Send sample ASAP to the laboratory as prolonged storage affects DNA extraction</td>
<td>No service provided</td>
<td>Any time providing sufficient DNA is available</td>
<td>Urgent: 3-10 days</td>
</tr>
<tr>
<td>Haemoglobinopathy Genetic Modifiers</td>
<td>10mls EDTA</td>
<td>Not applicable</td>
<td>Delay in receiving sample</td>
<td>Restriction enzyme PCR, DNA sequencing, MLPA. Send sample ASAP to the laboratory as prolonged storage affects DNA extraction</td>
<td>No service provided</td>
<td>Any time providing sufficient DNA is available</td>
<td>Urgent: 10 days</td>
</tr>
<tr>
<td>Prenatal Diagnosis for the haemoglobin disorders</td>
<td>10-20mg chorionic villus tissue in sterile culture medium or 10mls</td>
<td>Not applicable</td>
<td>Delay in receiving sample</td>
<td>Detection of mutations by ARMS-PCR, Restriction Enzyme PCR, Gap-PCR, DNA sequencing, MLPA. Detection of maternal contamination by 15 polymorphic STR markers. Send sample ASAP to the laboratory as prolonged storage affects DNA</td>
<td>No service provided</td>
<td>Any time providing sufficient DNA is available</td>
<td>Urgent 3 days</td>
</tr>
<tr>
<td>amniotic fluid in sterile container or 2mls Fetal blood in EDTA</td>
<td>extraction</td>
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