National Haemoglobinopathy Reference Laboratory

Information for Users

Summary

The NHRL offers a service for the identification of haemoglobinopathy genotypes by the molecular analysis of DNA and haematological investigation. This includes the investigation of difficult/complex phenotypes and the identification of carrier states for antenatal patients. It also offers a prenatal diagnosis service by fetal DNA analysis.

Haemoglobinopathy investigations are also undertaken as part of molecular testing for rare inherited anaemias.

Opening Times. The NHRL is staffed from 9.00 to 17.00 hours, Mon–Fri, except for bank holidays.
To contact the laboratory please phone 01865 572769 or email oxford.molecularhaem@nhs.net
Further information and referral forms are available on our website: https://www.oxford-translational-molecular-diagnostics.org.uk/

1) NHRL Tariffs and target turnaround times (TAT):

The current tariffs for the diagnostic services provided by the NHRL are:

Charge £	***Type of report***	***Target TAT*** *(from sample receipt in lab)*
50	*Haematology only (includes FBC, HPLC, IEF where appropriate)*: interpretation of results	3 working days for urgent neonates 14 working days for other samples
250	*Haematology (as above) & DNA testing* DNA sequencing of alpha and beta globin genes, alpha globin gene locus MLPA and further testing where deemed appropriate (eg.beta globin gene locus MLPA, sequencing of the gamma and delta globin genes)	42 calendar days for routine samples 21 calendar days for urgent antenatal or neonatal referrals
500	*Haematology & DNA testing for rare anaemia:* Haematology as above Haemoglobinopathy investigations as above Next generation sequencing of 51 additional genes associated with rarer genetic disorders involving anaemia (requires a different referral form)	84 calendar days for routine samples 42 calendar days for single gene family tests 21 calendar days for urgent antenatal or neonatal referrals
1150	*Prenatal diagnosis* *Haematology & DNA testing of fetus and parents* Predictive genetic testing of the fetus based on the parental genotypes. Includes parental genetics and haematology and test for maternal contamination	3 calendar days where the mutations in both parents are known in advance Up to 21 calendar days where the mutations are not known or if the father is not available for testing

The NHRL was centrally funded by the DH from 1982 to 31st March 2006, after which the central funding ceased and the DH required the NHRL to charge for its service on a provider to provider basis. Our central funding was devolved to all PCTs to pay for haemoglobinopathy DNA studies. However central funding will soon (most likely 2020) be provided by NHSE for individuals living in England meeting the referral criteria (please see https://www.england.nhs.uk/publication/national-genomic-test-directories/)

Invoicing

Invoices will be sent monthly from the Oxford University Hospitals Trust Finance Department to you, or the nominated contact provided by you on the referral form.

2) Sample Referral Procedures

Ideally fresh 2 x 4*ml EDTA blood sample labelled with the patient's forename, surname, date of birth and NHS number (if appropriate) should be sent with:

a. a completed genotype referral request form with patient information clearly supplied
b. haematological results from the patient must include a full blood count and if possible Hb A_2 and F values, iron status, Hb electrophoresis results eg HPLC.

For optimal DNA analysis results, blood samples should be less than 5 days old. However samples up to one month old that have been kept refrigerated may give satisfactory results.

*DNA extraction can be attempted from blood samples of 0.5-2ml but may not provide adequate amounts of DNA to complete complex analyses.

DNA extracted elsewhere is also accepted for genetic testing, but it is **ESSENTIAL** that the red cell indices and protein analysis (HPLC or similar) is provided for these samples to enable full interpretation of the genetic results in the context of the phenotype.

There are separate referral forms for genotype analysis and prenatal diagnosis (available for download from our website: https://www.oxford-translational-molecular-diagnostics.org.uk/content/forms. The referral form must be filled in and returned with the samples.

Samples should always be sent in appropriate packaging by first class post, or for urgent samples, by courier service. **All non-PND referrals should be sent to the following address (See 'Prenatal diagnosis requests section' for address to send PND samples :**

Moira Wicks,
Molecular Haematology,
Level 4,
John Radcliffe Hospital,
Headington,
Oxford,
OX3 9DU

Prenatal diagnosis request:

The lab must be telephoned in advance to make arrangements for the referral of a prenatal diagnosis case, including provision of secure contact details to report the result by telephone and email.

Requirements: Ideally 2 x 4ml fresh parental EDTA blood samples (or extracted parental DNA) must be sent with the fetal sample, together with a completed prenatal diagnosis request form with the following parent information clearly supplied: haematological results from both parents (full blood count, Hb A_2 and F values, Hb electrophoresis results).

If the father is unavailable for blood sampling, a copy of his laboratory results stating his haemoglobin genotype should be provided (ideally from a UKAS accredited laboratory). ***If the paternal genotype is unknown please advise the mother that the PND test is offered on a at risk basis only and that turn-around-time (TAT) is likely to be longer.***

Fetal sample: To ensure the most rapid and efficient testing, DNA extracted from CVS, amniotic fluid or fetal blood* should be provided for prenatal diagnosis (with the parental samples)

If it is not possible to send fetal DNA the following samples are acceptable:

- **Chorionic villus biopsy sample (CVS):** The CVS **must** be cleaned by microscopic dissection to remove any contaminating maternal tissue before sending to the address above for DNA analysis. The referrer must arrange for this to be carried out at a local cytogenetics laboratory, and also instruct the lab to forward the sorted CVS by guaranteed post or courier.

  It is recommended that a CVS culture is set up by the cytogenetics lab for back up purposes if this is not to be done routinely by the lab for karyotyping. The NHRL will contact the cytogenetic laboratory if the backup cultures are required.

  The cleaned CVS should be sent to the Oxford Regional Genetics Laboratories (RGL) in culture medium.

- **Amniotic fluid sample:** Obstetric departments should aim to take >20 mls of amniotic fluid. At least 10mls can then be forwarded directly to the RGL for testing. The remaining ~10 mls can be sent to a local cytogenetics laboratory for back-up cultures. The NHRL will contact the cytogenetic laboratory if the backup cultures are required. If it is not possible to obtain 20mls of amniotic fluid please telephone the laboratory for advice.

- **Fetal blood:** On very rare occasions fetal blood sampling may be performed and a fetal blood sample sent in EDTA for analysis. For example, for the diagnosis of homozygous alpha^0-thalassaemia in a fetus diagnosed as hydropic by ultrasound.

All PND related samples (both the fetal and parental samples) should be sent to the following address:

Rachel Roche
Oxford Regional Genetics Laboratories,
Oxford University Hospitals NHS Foundation Trust
The Churchill Hospital
Oxford
OX3 7LE

Patient Consent:

Patient consent should be obtained for obtained for medical investigations for a haemoglobinopathy/rare anaemia. This permits the referral of the blood sample to another laboratory for: additional investigations of the haemoglobinopathy, the storage of the patient's DNA sample for any further investigations related to the patient's diagnosis in the future, the use of the patient's DNA for quality assurance in laboratory tests, and the use of the patient's DNA for education and training of laboratory staff. It will not permit the analysis of the patient's DNA for any other genetic disorder without further specific consent for that test.

Quality Assurance

The NHRL participates in the NEQAS "DNA diagnostics for haemoglobinopathies" scheme, the NEQAS "Hb A_2/Hb F & abnormal haemoglobins" scheme, newborn sickle screening scheme and the NEQAS full blood count scheme. We also participate in the NEQAS schemes for maternal contamination, NGS panels and pathogenicity investigation.

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Dr Noemi Roy

Principal Clinical Scientist (Haemoglobinopathies and rare anaemias): Melanie Proven

Address (correspondence & non PND referrals): Molecular Haematology, Level 4, John Radcliffe Hospital, Headington, Oxford, OX3 9DU
Sample reception: 01865 572769 Sec: 01865 572826 Fax: 01865 572775
Email: oxford.molecularhaem@nhs.net.
Web site: http://www.oxford-translational-molecular-diagnostics.org.uk/