Bristol Genetics Laboratory is a UKAS accredited medical laboratory No.9307.

North Bristol NHS Trust's Department of Immunology and Immunogenetics is a UKAS accredited medical laboratory No.8067.

North Bristol NHS Trust

GATA1 Diagnostic Service for Myeloid Proliferations Related to Down Syndrome

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Sample(s) Required:
See Sample requirements page at www.nbt.nhs.uk/genetics for full details

Blood: at least 1ml in EDTA
An unstained blood film (if morphological review is required)

Samples should be accompanied by a FULLY completed request form (available as download at www.nbt.nhs.uk/genetics or from the laboratory).

Please include details of the test required, family history, address including postcode, NHS number, referring clinician and centre.

Consent and Storage:
All genetic testing requires consent. **It is the responsibility of the referring clinician to ensure that appropriate consent has been obtained.**

DNA is stored from **ALL** patients undergoing DNA testing, unless consent for this is specifically denied.

Stored material from all referrals may be retained for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Clinical Background and Genetics

- Between 5-30% of children with Down syndrome (DS) are born with transient abnormal myelopoiesis (TAM).
- Whilst many TAM cases resolve without treatment, TAM results in early death in 15-23% cases and 20-23% of survivors develop myeloid leukaemia of Down syndrome (ML-DS) in the first 4 years of life.
- TAM is driven by mutations in the haematopoietic transcription factor gene *GATA1* and is only seen in conjunction with trisomy 21.
- All cases of TAM and ML-DS are marked by the presence of an acquired N-terminal mutation in *GATA1*, resulting in a truncated GATA1 protein (GATA1s).

Service Offered
The Bristol Haemato-Oncology Service (BHODS) offers integrated diagnostic testing for myeloid proliferations related to Down syndrome.

Molecular testing: *GATA1* analysis is offered by a sensitive next generation sequencing assay.

Flow cytometry: The blasts in neonates with DS have an immunophenotype that is distinct from other leukemic and normal progenitor cells. Whilst this cannot identify *GATA1* mutated cells from blasts without a *GATA1* mutation it does allow accurate quantitation of the blast count by flow cytometry in these cases.

Morphology: Specialist clinical advice and review of morphology is available from expert clinicians at the Bristol Royal Hospital for Children.

Indications for *GATA1* Analysis
Guidance from the British Society of Haematology (Tunstall *et al*., 2018) recommends *GATA1* analysis for the following indications:

- Neonates with a blast percentage >10% and/or clinical features suggestive of TAM
- Relapse/suspected relapse of TAM
- ML-DS/suspected ML-DS
- Clinical features on foetal ultrasound scanning suggestive of TAM.

Referrals
Referrals are accepted from Consultant Neonatologists, Paediatricians and Haematologists.

Clinical Advice: If clinical discussion is required, we would recommend contact with Dr Oliver Tunstall, Consultant Paediatric Haematologist at Bristol Royal Hospital for Children (Tel: 0117 342 8752)

Target Reporting Times

- Anticipated reporting time: 21 days from receipt of the sample.

Quality

- Bristol Genetics Laboratory participates in the EMQN and NEQAS external quality assurance schemes for sequencing and variant analysis.

Please contact the laboratory for up to date prices

Reference
Tunstall, O. *et al*. Guidelines for the investigation and management of Transient Leukaemia of Down Syndrome. *British Journal of Haematology, 182, 200–211, (2018)*

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