Clinical Background and Genetics
- Between 5-30% of children with Down syndrome (DS) are born with transient leukaemia of Down syndrome (TL-DS).
- Whilst many TL-DS cases resolve without treatment, TL-DS 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.
- TL-DS is driven by mutations in the haematopoietic transcription factor gene GATA1 and is only seen in conjunction with trisomy 21.
- All cases of TL-DS 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
Recent 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 TL-DS
- Relapse/suspected relapse of TL-DS
- ML-DS/suspected ML-DS
- Clinical features on foetal ultrasound scanning suggestive of TL-DS.

The guidelines also suggest considering GATA1 analysis for:
- The follow up of individuals with a known GATA1 variant and persistent full blood count abnormalities.

Target Reporting Times
- Anticipated reporting time: 42 days from receipt of the sample.
- Samples must arrive at the laboratory by 2.30pm to be processed on the day of receipt.

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