Bristol Genetics Laboratory

North Bristol NHS Trust

GATA2 Sequence Analysis

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Sample Required:
Adult: 5mls blood in EDTA
Paediatric: at least 1ml EDTA (preferably >2ml)

Prenatal testing MUST be arranged with the laboratory well in advance.

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 test, family history, address and POSTCODE, NHS number, referring clinician and unit/hospital.

Consent and DNA 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 unless consent for this is specifically denied.

Stored samples may be used for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Clinical Background

- Germline mutations in the *GATA2* gene are associated with several phenotypes:
  - Dendritic cell, monocyte, B lymphocyte, and natural killer lymphocyte deficiency (DCML)
  - Monocytopenia with susceptibility to mycobacterial, fungal, and papillomavirus infections and myelodysplasia (MonoMAC syndrome)
  - Primary Lymphedema With Myelodysplasia / Emberger syndrome
  - Susceptibility to Acute Myeloid Leukaemia & Myelodysplastic syndrome
- The protein encoded by the *GATA2* gene plays an essential role in regulating transcription of genes involved in the development and proliferation of hematopoietic and endocrine cell lineages.
- Inherited or *de novo* mutations in *GATA2* can cause wide phenotypic variability including a complex congenital disorder characterised by immunodeficiency, bone marrow failure, and lymphatic/vascular dysfunction. Patients may also suffer from severe and recurrent infections, myelodysplasia/leukaemia, pulmonary alveolar proteinosis, lymphedema, sensorineural hearing loss, and possibly susceptibility to other malignancies, autoimmune disorders, thrombotic events, and miscarriage.
- Age at presentation can vary. Reduced penetrance and variable expressivity is also observed.

Referrals

Diagnostic Testing: Coding exons (including flanking intronic sequences and predicted branch points) and a conserved intronic element of the *GATA2* gene are sequenced using Sanger sequencing with an assay sensitivity of >95%.

- Referrals are accepted from Consultant Haematologists, Consultant Oncologists and Clinical Geneticists in patients with the following criteria:
- Recurrent, unexplained severe or prolonged mycobacterial, HPV, EBV or fungal infections or myelodysplastic syndrome AND at least one of the following:
- Lymphocyte subset analysis showing reduced numbers of NK cells ± B cells
- Primary lymphedema
- Sensorineural deafness
- Monocytopenia
- Evidence of familial MDS/AML
- At risk family members where familial mutation is known.

Carrier Testing: Testing of parental samples is offered once the mutations have been identified in the affected patient. Cascade testing can also be undertaken on close adult relatives and siblings

Prenatal diagnosis: Please contact the laboratory to discuss.

	Target reporting Time
Full Gene Screen	56 days
Familial Mutation Testing	14 days
Prenatal Diagnosis	3 days (Contact laboratory to arrange)

For current prices please contact the laboratory

Quality: This laboratory participates in the following external quality assurance schemes which cover the technique and strategies used for this service: EMQN Sanger DNA sequencing scheme and UKNEQAS Pathogenicity of sequence variants interpretation scheme.

Clinical Advice: Please contact Dr Colin Steward, Consultant in BMT, Genetic and Metabolic Disease, Royal Hospital for Children, Bristol. Tel: 0117 342 8044. Email: colin.steward@uhbristol.nhs.uk

DETAILS CORRECT AT DATE OF PRINTING ONLY.
Active date of this version: 18/03/2019
Approved by: Laura Yarram-Smith
Version: 3
Information 79 BGL Service Proforma for GATA2 Mutation Analysis

Exceptional healthcare, personally delivered

CPA
Accredited Medical Laboratory
Reference No: 2907