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

North Bristol NHS Trust

Familial Paroxysmal Kinesigenic Dyskinesia and associated disorders

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

Samples should be accompanied by a FULLY completed request form (available as download at https://www.nbt.nhs.uk/south-west-genomic-laboratory-hub or from the laboratory).

Please include details of test, family history, address and POSTCODE, NHS number, referring clinician and unit/hospital.

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

- Mutations in *PRRT2* are associated with three autosomal dominant neurological conditions characterised by afebrile seizures and various degrees of dystonia:
  - **Familial Paroxysmal Kinesigenic Dyskinesia** - **EKD1** (OMIM 128200)
  - **Benign Familial Infantile Convulsions with Paroxysmal Choreoathetosis** - **ICCA** (OMIM 602066)
  - **Benign Familial Infantile Convulsions** - **BFIS2** (OMIM 605751)
- EKD1 is characterized by recurrent and brief attacks of involuntary movement, triggered by sudden voluntary movement. These attacks usually have onset during childhood or early adulthood and can involve dystonic postures, chorea, or athetosis. Symptoms become less severe with age and show favourable response to anticonvulsant medications such as carbamazepine or phenytoin.
- In BFIS and ICCA, the average onset of seizures is 6 months.
- The *PRRT2* gene is located on chromosome 16p11.2 and consists of 4 exons, the first of which is not coding. The protein encoded by *PRRT2* has 340 amino acids and is predicted to have two transmembrane segments; the function of which is currently unknown.
- *PRRT2* mutations show variable penetrance, ranging from 60-90% depending on clinical context.
- The c.649dupC mutation is the most common *PRRT2* mutation reported to date.

Service offered

- Analysis of all coding exons (exons 2-4) of the *PRRT2* gene by direct Sanger sequence analysis

Referrals

- **Diagnostic testing:** to confirm a diagnosis in a patient showing clinical symptoms of EKD1, BFIS or ICCA. Referrals are accepted from Consultant Neurologists or Consultant Clinical Geneticists.
- **Carrier testing:** available for relatives once the mutation has been identified in the proband, if appropriate. Requests accepted from Clinical Genetics only.

Target Reporting Time and Indicative Cost

PRRT2 Full gene screen	42 calendar days
Testing for known mutation	42 calendar days
Predictive testing	14 calendar days

Please contact the laboratory for up to date prices.

Quality

BGL participates in the external quality assurance EMQN for Sequencing QA scheme and for Variants of Unknown Clinical Significance interpretation scheme.

Clinical Advice

If clinical discussion is required we would recommend contact with Dr Sarah Smithson, Consultant Clinical Geneticist Tel: 0117 342 5316, or Dr Phil Jardine Consultant Paediatric Neurologist Tel: 0117 342 0167.

Information document No.76 , Version 5
Active date of this version: 04/11/2020
DETAILS CORRECT AT DATE OF PRINTING ONLY.
Approved by: Anthony Dallosso