Bristol Genetics Laboratory

North Bristol NHS Trust

KBG Syndrome

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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 to 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 and Genetics

- KBG syndrome (OMIM #148050) is a rare autosomal dominant/sporadic disorder characterized by intellectual disability associated with macrodontia of the upper central incisors as well as distinct craniofacial findings, short stature, and skeletal anomalies.
- Less than one hundred cases of KBG syndrome have been reported to date and it is considered to be likely to be underdiagnosed as many of the features are mild and none are a pre-requisite for diagnosis. To date, the incidence of diagnosed males is far higher than that of females. Transmission from mildly affected parents (usually the mother) has been reported.
- Mutations or deletions of the *ANKRD11* gene have been demonstrated to cause KBG syndrome. Copy number variation in the 16q24.3 region that includes *ANKRD11* results in a variable phenotype that overlaps with KBG syndrome.
- Sanger sequencing of the entire coding region of the *ANKRD11* gene will detect a likely pathogenic variant in a significant proportion of cases clinically diagnosed as affected by a clinical geneticist. Larger intragenic deletions and duplications may not be detected. Array CGH analysis should be considered for mutation negative cases.

Service offered

- Bidirectional sequence analysis of the full coding region of *ANKRD11* which should detect all of the missense, nonsense and small indel mutations published to date.
- Familial tests for known mutations.
- Confirmation of mutations detected in research settings e.g. DDD.

Referrals

- **Diagnostic Testing**: Referrals meeting UKGTN clinical testing criteria accepted from Consultant Clinical Geneticists.
- **Carrier Testing:** Accepted from Consultant Clinical Geneticists. Please provide details of affected patient and known mutation.

Quality

- This laboratory participates in the EMQN Sanger DNA sequencing scheme.
- A gene dossier was submitted to UKGTN approval in the 2014/5 cycle.

Target reporting Time & Cost

Full gene screen	56 days
Known mutation	28 days

Please contact laboratory for up-to-date prices

Clinical Advice

We recommend contact with **Dr Sarah Smithson** Consultant Clinical Geneticists, Level B St Michael's Hospital, Bristol BS2 8EG (Tel: 0117 342 5558; e-mail sarah.smithson@uhbristol.nhs.uk).

Information document No. Version 2
Active date of this version: 19/07/2016
DETAILS CORRECT AT DATE OF PRINTING ONLY.
Approved by: M Williams

CPA
Accredited Medical Laboratory
Reference No: 2907