**KBG Syndrome**

**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**

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<thead>
<tr>
<th>Test Type</th>
<th>Reporting Time</th>
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<tbody>
<tr>
<td>Full gene screen</td>
<td>56 days</td>
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<tr>
<td>Known mutation</td>
<td>28 days</td>
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**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).