FAMILIAL LONG QT SYNDROME (JERVELL & LANGE-NIELSEN SYNDROME)
Genes (OMIM): KCNQ1 (607542), KCNE1 (176261)

INTRODUCTION
Autosomal recessive long QT syndrome, Jervell & Lange-Nielsen Syndrome (JLNS), is an inherited disorder of ventricular repolarisation. It has an estimated prevalence of 1 in 1,000,000 individuals. It is characterised by a prolonged QT interval on ECG (typically >500ms) with congenital sensorineural deafness. This recessive form of long QT syndrome is usually more severe than the autosomal dominant form, and can result in sudden death before 15 years of age if left untreated. Mutations in two cardiac potassium ion channel genes, KCNQ1 and KCNE1, are known to predispose to JLNS10.

REFERRAL PROCEDURE
• Diagnostic referrals are accepted for probands with a suspected or confirmed diagnosis of Jervell and Lange-Nielsen syndrome.
  o Referrals are accepted from Cardiology, Clinical Genetics and other relevant medical specialities.
  o Clinical information and details of relevant family history should be provided with all referrals either on the original request form or on a separate pre-referral form (Cardiac Arrhythmia Pre-referral form).
• Family test referrals are only accepted from Clinical Genetics specialists.
  o Referrals for affected family members (i.e. segregation analysis) must be accompanied by appropriate clinical information.
  o Referrals for unaffected family members will only be considered for variants with clear evidence for pathogenicity.
• Clinical advice is available from Dr Edward Blair, Consultant Clinical Geneticist, at the Churchill Hospital (Ed.Blair@ouh.nhs.uk).
• Further information about the test can be obtained from the laboratory (OxfordCardiac@nhs.net).

Sample Requirements
• This analysis requires 3 µg of DNA, preferably at >100 ng / µl.
• Blood samples, including post-mortem blood (provided it is not clotted) is suitable (1-5ml EDTA).
  N.B. Cord blood samples should be accompanied by a maternal sample.
• Fresh or frozen tissue - generally spleen although other tissues are acceptable (1cm cubed)
• Formalin-fixed paraffin-embedded (FFPE) will be accepted for panel testing but poor quality of extracted DNA from these samples may mean analysis is not possible or coverage is lower than quoted. In general, Sanger gap filling is not usually possible from this material.

Testing Strategy
Molecular analysis is undertaken by fluorescent dideoxy sequencing of the exons and intron/exon boundaries of the KCNQ1 (exons 1–16) and KCNE1 (exon 1) genes. Dosage analysis of both genes by multiplex ligation-dependent probe amplification (MLPA) can also be undertaken as a separate test on request.

Target Reporting Times and Prices

<table>
<thead>
<tr>
<th>Referral Type</th>
<th>Molecular Analysis</th>
<th>Target Reporting Time (working days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic</td>
<td>Sequence analysis of KCNQ1 and KCNE1</td>
<td>40</td>
</tr>
<tr>
<td>Diagnostic</td>
<td>MLPA dosage analysis of KCNQ1 and KCNE1</td>
<td>10</td>
</tr>
<tr>
<td>Familial</td>
<td>Familial mutation(s)</td>
<td>10</td>
</tr>
</tbody>
</table>

• Please see the current price list on the Oxford Genetics laboratory Molecular genetics page


N.B. Details are correct for the date of printing only. Last updated August 2015