Legius Syndrome (NFLS, Neurofibromatosis Type 1-like Syndrome) – OMIM 611431

Background
Legius syndrome is found in some people who have mild NF1-type symptoms, but have no mutation in the \textit{NF1} gene (OMIM 613113). This condition is caused by a mutation in a different gene, \textit{SPRED1} (OMIM 609291), and while freckling or café-au-lait patches can be present, there are usually no tumours or neurofibromas, and less likelihood of severe complications from the condition. Some patients with Legius syndrome suffer from learning difficulties and hyperactivity. The condition follows an autosomal dominant inheritance pattern so an affected adult has a 50% chance of having an affected child. Initial estimates of incidence were approximately 1/150000, but a recent study of \textit{NF1} gene-negative patients detected approximately 3%, making the incidence more in the region of 1/100000.

Recommended Clinical Referral Criteria
- Patients with NF1-like symptoms that do not have a mutated \textit{NF1} gene
- Family history

Molecular Analysis

<table>
<thead>
<tr>
<th>Mutation screen</th>
<th>Bi-directional sequence analysis and MLPA dosage analysis of the entire coding region of the \textit{SPRED1} gene; data from our patient cohort since 2009 shows (2/45) 4% have had a pathogenic change detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family follow-up</td>
<td>Testing for known familial mutations in \textit{SPRED1} gene</td>
</tr>
</tbody>
</table>

Prices* & Turnaround Times (TAT)
* Valid until March 2019 - prices apply to NHS referrals; non-NHS patients are subject to 20% surcharge

| Test | TAT(working days) | Price *
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Test for known familial mutations in \textit{SPRED1} - single sample (multiple samples sent together – price per sample)</td>
<td>20</td>
<td>£160 (£90)</td>
</tr>
<tr>
<td>Mutation screening and dosage analysis (\textit{SPRED1})</td>
<td>40</td>
<td>£250</td>
</tr>
</tbody>
</table>

Sample Requirements
- Blood – 5ml in EDTA (1ml neonates/infants);
- Please contact lab prior to sending a prenatal sample;
- Please label samples with three identifiers and date of collection.

All samples must be accompanied by request form
- Consent for testing & DNA storage is assumed when request for test received

Contact Details
All Wales Genetics Laboratory,
Institute of Medical Genetics,
University Hospital of Wales,
Heath Park,
Cardiff CF14 4XW
Tel: 029 2074 2641
Fax: 029 2074 4043
lab.genetics@wales.nhs.uk
http://www.wales.nhs.uk/AWMGS/
Accredited to ISO 15189:2012 (8988)

Links
- UKGTN http://ukgtn.nhs.uk/
- Orphanet http://www.orpha.net/
- EDDNAL http://www.eddnal.com/
- OMIM http://www.omim.org/

Support
(no support group for Legius but here are a couple for NF)
- www.nfauk.org
- http://www.ctf.org/

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