Amyotrophic Lateral Sclerosis (ALS) – OMIM 105400; Frontotemporal Dementia (FTD) – OMIM 600274

Background
1 in 50,000 people have motor neuron disease (MND). Amyotrophic lateral sclerosis (ALS) is a form of MND characterized by the death of motor neurons in the brain, brainstem and spinal cord. This leads to wasting in the limbs and progressive paralysis, and there are no effective therapies – it is fatal due to eventual respiratory failure, typically two to three years after the onset of symptoms. Around 5% of ALS cases are familial (inherited). Frontotemporal dementia (FTD) is a relatively common cause of dementia in younger patients but is overall less common than Alzheimer disease or Cortical Lewy body disease. Symptoms vary but can include behavioural and personality changes, problems with language skills and inability to plan or organize complex tasks. There is evidence to suggest that there is an overlap with these ALS and FTD as symptoms of both conditions can occur in the same patient, in the same families and as alternative presentations of pathogenic C9ORF72 (OMIM 614260) mutations. The recent discovery of large 6bp repeat expansions in chromosome 9 open reading frame 72 (C9ORF72 – chromosome location 9p21) is diagnostic of familial ALS and FTD, and may also be used as a predictive test for at-risk familial members [Ref. Neuron 2011, 72(2); 257-68]. Mutations in MAPT, GRN, TARDP and UBQLN2 genes, among others, may cause similar clinical syndromes.

Recommended Clinical Referral Criteria
- Affected patients with a family history of either or both of these disorders
- At-risk family members with a known familial mutation for predictive testing
- We are also interested in receiving samples from familial cases on a research basis to look for further genes

Molecular Analysis

Gene fragment analysis: Fragment length analysis of C9ORF72 [GGGGCC] hexanucleotide repeat expansion by PCR and repeat-primed PCR, or by Southern blot; this mutation is found in approximately 40% of familial ALS cases and 23% of familial FTD cases.

Family follow-up: Testing for known familial mutations in C9ORF72 gene

Prices* & Turnaround Times (TAT)
* Valid until March 2017 - prices apply to NHS referrals; non-NHS patients are subject to 20% surcharge

<table>
<thead>
<tr>
<th>Test</th>
<th>TAT(working days)</th>
<th>Price</th>
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<tbody>
<tr>
<td>Testing for familial mutation in C9ORF72 – single sample</td>
<td>20</td>
<td>£160</td>
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<tr>
<td>(multiple samples sent together – price per sample)</td>
<td></td>
<td>(£90)</td>
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<tr>
<td>C9ORF72 expansion analysis (PCR)</td>
<td>20</td>
<td>£160</td>
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<tr>
<td>C9ORF72 expansion analysis (Southern blot) – please contact the lab</td>
<td>40</td>
<td>£160</td>
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<td>prior to sending sample</td>
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<tr>
<td>C9ORF72 expansion analysis – complete service (PCR, then Southern</td>
<td>40</td>
<td>£200</td>
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<td>blot if required)</td>
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Contact Details
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http://www.wales.nhs.uk/AWMGS/ (CPA Accredited - 2381)

Sample Requirements
Blood – 5ml in EDTA (10-12 µg of DNA required for Southern blot)
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

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