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 behavioral 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

Molecular Analysis

Gene fragment analysis: Fragment length analysis of *C9ORF72* [GGGGCC] hexanucleotide repeat expansion by PCR and repeat-primed PCR; 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

AWMGS
All Wales Medical Genomics Service

Test (Price available on request)	TAT
Testing for familial mutation in *C9ORF72*	28cd
Diagnostic *C9ORF72* expansion analysis	42cd

Contact Details
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Accredited to ISO 15189:2012
(8988)

Sample Requirements
Blood – 5ml in EDTA

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

Orphanet
http://www.orpha.net/
EDDNAL
http://www.eddnal.com/
OMIM
http://www.omim.org/
Gene Test Registry
http://www.ncbi.nlm.nih.gov/gtr/
Support
http://www.mndassociation.org