

## Fragile X (A) syndrome (OMIM# 300624)

### Background

Fragile X (A) is an X-linked disorder and the most common single-gene cause of inherited learning disabilities. Over 99% of cases are caused by an expansion of a CGG repeat in the 5'UTR of the gene *FMR1* (OMIM\* 309550), resulting in methylation and silencing of the gene.

The condition predominantly affects males (approximately 1 in 4000-6000), where it causes moderate to severe intellectual and social impairment with syndromic features including large ears and head, long face and macroorchidism.

Females with a full expansion have a variable phenotype from phenotypically unaffected (~50% of cases) to moderate mental and social impairment.

### Recommended Clinical Referral Criteria

- **Diagnostic testing (Paediatric or Clinical Genetics referrals)**
  - Diagnostic testing for patients with learning disability will usually only take place following a normal array CGH result. Please refer to the array CGH referral criteria for children with learning disabilities
- **Family testing (Clinical Genetics referrals)**
  - Relatives with a confirmed family history of Fragile X or *FMR1* related disorder
- **Prenatal testing** is carried out at the Manchester Centre for Genomic Medicine ([www.mangen.co.uk](http://www.mangen.co.uk))

### Molecular Analysis

- 1) **FRAXA PCR Assay:** Fragment length analysis of *FMR1* gene [CGG]<sub>n</sub> triplet repeat. Pre-screen for the majority of diagnostic referrals.
- 2) **Asuragen Amplidex PCR Assay:** Fragment length analysis of *FMR1* gene [CGG]<sub>n</sub> triplet repeat expansions in pre-mutation and full mutation size range by CGG repeat primed PCR analysis.

### Prices\* & Turnaround Times (TAT)

\* Prices available on request

Test	TAT
<i>FMR1</i> expansion analysis (PCR)	42cd
<i>FMR1</i> high sensitivity gene expansion analysis	42cd

#### Contact Details

All Wales Genomics Laboratory,  
Institute of Medical Genetics,  
University Hospital of Wales,  
Heath Park,  
Cardiff CF14 4XW  
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[www.medicalgenomicswales.co.uk](http://www.medicalgenomicswales.co.uk)  
Accredited to ISO 15189:2012

#### 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.

#### Links

**Orphanet**  
<http://www.orpha.net/>  
**EDDNAL**  
<http://www.eddnal.com/>  
**OMIM**  
<http://www.omim.org/>  
**Genetic Test Registry**  
<http://www.ncbi.nlm.nih.gov/gtr/>  
**Support**  
[www.fragilex.org.uk](http://www.fragilex.org.uk)

