**Fabry disease (α-galactosidase A deficiency)**

**Introduction**

Fabry disease (MIM 301500) is an X-linked lysosomal storage disorder affecting ~1/40,000 males. It is due to a deficiency of the lysosomal hydrolase, α-galactosidase A. Males with classical Fabry disease have no residual enzyme activity, whereas atypical patients, usually with symptoms confined to the heart (cardiac variant), have varying degrees of residual activity. These enzyme activity levels allow the clinical diagnosis to be confirmed. The symptoms of Fabry disease begin during childhood or teenage years and include angiokeratoma, acroparesthesia and ocular features. Cerebrovascular, cardiovascular and renal malfunction may develop later. Clinical manifestation in carrier females can range from being asymptomatic to being as severely affected as affected males. Enzyme replacement therapy for Fabry disease is now well established and in wide use.

The gene encoding α-galactosidase A (GLA) (Xq22.1) consists of 7 exons and family specific mutations are found throughout the gene, although some recurrent mutations are reported and one mutation, p.(Asn215Ser), is commonly found in patients with the cardiac variant.

**Referrals**

- Clinically affected male patients should have their diagnosis confirmed by biochemical analysis; this should be arranged either locally or with the Enzyme Unit, Chemical Pathology, Great Ormond Street Hospital (tel: 0207 4059200 ext 1785/6751). Biochemically confirmed patients can be referred for mutation analysis.
- Clinically affected female patients can be referred directly for mutation analysis (due to unreliability of heterozygote detection by biochemical testing).
- Mutation testing can be offered to relatives of affected patients once a disease causing mutation has been identified.

**Prenatal testing**

Prenatal testing is available, if required, for families where specific mutations have been identified - please contact the laboratory to discuss.

**Service offered**

Mutation screening of all 7 exons and intron-exon boundaries of the GLA gene is undertaken by Sanger sequence analysis in affected patients followed by MLPA dosage analysis to detect large deletions/duplications of the GLA gene.

Mutation specific testing for previously identified mutations is also available in family members.

**Target reporting time**

8 weeks for routine mutation screen (including MLPA) in index case. 2 weeks for family mutation specific tests. Please contact the laboratory for urgent cases.