NE THAMES REGIONAL MOLECULAR GENETICS SERVICE
X-Linked lymphoproliferative disease (XLP)

Contact details

Molecular Genetics
GOSH NHS Trust
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+44 (0) 20 7813 8196

Samples required

For DNA analysis only: 5ml venous blood (pre-BMT) in plastic EDTA bottles (>1ml from neonates)

Prenatal testing must be arranged in advance, through a Clinical Genetics department if possible.

Amniotic fluid or CV samples should be sent to Cytogenetics for dissecting and culturing, with instructions to forward the sample to the Regional Molecular Genetics laboratory for analysis

A completed DNA request card should accompany all samples.

Introduction
XLP 1 (MIM 308240) and XLP 2 (MIM 300635) are X-linked immunodeficiencies characterised by extreme sensitivity to the Epstein Barr virus (EBV). Affected individuals can be diagnosed on the basis of an abnormality or deficiency of the SLAM associated protein (SAP) or XIAP protein. The SH2D1A gene (encoding for SAP) has 4 exons and family specific mutations are found throughout the gene. The XIAP gene has 7 exons (6 coding). The guidelines for the NCG service for immunodeficiencies apply to the molecular analysis of XLP (details on request).

Referrals

- Affected patients should be referred to the Molecular Immunology department at GOSH for SAP/XIAP protein analysis. This requires prior arrangement and completion of specific request forms (see contact information below). We work closely with this department and are able to undertake mutation screening in appropriate patients.
- Carrier testing can be offered to the female relatives of XLP patients once a disease causing mutation has been identified.

Prenatal testing
Prenatal testing is available for families in whom specific mutations have been identified or in whom appropriate family studies have been undertaken - please contact the laboratory to discuss.

Service offered
Mutation screening of the SH2D1A or XIAP genes in affected individuals found to have no/abnormal SAP or XIAP expression. Cases found to have SAP or XIAP expression may be screened if there is a strong clinical indication for a diagnosis of XLP. If DNA from an affected male is unavailable screening can be undertaken in the mother. Mutation-specific tests for family mutations and linked marker analysis are also available.

Technical
Mutation screening is undertaken by sequence analysis of the 4 exons and exon/intron boundaries for the SH2D1A gene. This detects approximately 43% of mutations in patients shown to have abnormal or deficient SAP. This suggests that there is an as yet unidentified molecular defect in some of these patients, which may or may not be in the SH2D1A gene. In cases where we are unable to identify the mutation, linked marker analysis may be used to indicate carrier status and for prenatal diagnosis - please contact the laboratory to discuss.
Mutation screening of the 7 exons of the XIAP gene is undertaken by sequence analysis.

Target reporting time
2 months for routine mutation screen in index case. 2 weeks for carrier tests for known family mutations. For urgent samples please contact the laboratory.

To arrange SAP expression studies please contact Dr Kimberly Gilmour in Molecular Immunology, GOSH – Tel: +44 (0) 20 7829 8835, Email: gilmok@gosh.nhs.uk

Patient details
To facilitate accurate testing and reporting please provide patient demographic details (full name, date of birth, address and ethnic origin), details of any relevant family history and full contact details for the referring clinician