X-linked lymphoproliferative disease (XLP)

**Contact details**
Molecular Genetics Service  
Level 6, Barclay House  
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**Samples required**
- 5ml venous blood 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

**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

**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 SAP) has 4 exons and family specific mutations are found throughout the gene. The XIAP gene has 7 exons (6 coding).

**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 absent or 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 members 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.

Mutation screening of the 7 exons of the XIAP gene is undertaken by sequence analysis.

MLPA analysis for deletion/duplication analysis.

**Target reporting time**
8 weeks for routine mutation screen in index case. 2 weeks for carrier testing using mutation-specific tests. For urgent samples please contact the laboratory.

**To arrange SAP/XIAP expression studies please contact**
Dr Kimberly Gilmour, Molecular Immunology, GOSH  
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