NE THAMES REGIONAL MOLECULAR GENETICS SERVICE

X-linked Hyper IgM syndrome (HIGM)

Contact details

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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

Hyper IgM syndrome is a primary immunodeficiency characterised by an inability to produce immunoglobulin isotypes other than IgM and IgD resulting in susceptibility to bacterial and opportunistic infections. The disease is genetically heterogeneous with both X-linked recessive and autosomal recessive forms. X-linked HIGM (MIM 308230) is the most common form and affected individuals can be diagnosed on the basis of an abnormality or deficiency of the CD40 ligand protein, CD154. The CD40LG gene (MIM 300386) has 5 exons and family specific mutations are found throughout the gene. The guidelines for the NCG service for immunodeficiencies apply to the molecular analysis of X-linked HIGM (details on request).

Referrals

- Affected patients should be referred to the Molecular Immunology laboratory at GOSH for CD154 protein analysis. This requires prior arrangement and completion of specific request forms (see contact information below). We work closely with this department and will undertake mutation screening in appropriate patients.
- Carrier testing can be offered to the female relatives of X-linked HIGM 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 CD40LG gene in affected individuals found to have no/abnormal CD154 expression. Cases found to have CD154 expression may be screened if there is a strong clinical indication for a diagnosis of HIGM. If DNA from an affected male is unavailable screening can be undertaken in the mother. Mutation-specific tests and linked marker analysis are also available.

Technical

Mutation screening is undertaken by sequence analysis of the 5 exons and exon/intron boundaries. In cases where we are unable to identify the mutation, linked marker analysis may be used for family studies – Please contact the laboratory to discuss.

Target reporting time

2 months for routine mutation screen in index case. 2 weeks for carrier testing using mutation-specific tests. For urgent samples please contact laboratory.

To arrange CD154 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