Primary immunodeficiency (PID)

Contact details

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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

The primary immunodeficiencies (PID) are a heterogeneous group of >150 disorders that result from defects in immune system development and/or function. PIDs are broadly classified as disorders of adaptive immunity (i.e., T-cell, B-cell or combined immunodeficiencies) or of innate immunity (e.g., phagocyte and complement disorders).

The clinical presentation of PIDs is highly variable; however, most disorders involve increased susceptibility to infection. The type and pattern of infection depends on which part(s) of the host defences are missing or defective since some defences are more important against some pathogens than others. Defects in phagocyte function or humoral immunity (B cell deficiency) result in infections with common and unusual bacteria. Defects in T cell immunity usually present with recurrent viral, fungal, or protozoal infections. Very serious inherited immunodeficiencies become apparent shortly after birth or in the first year of life, and can lead to death if untreated. Others (usually the milder forms) may not present until people reach their twenties and thirties.

The minimum incidence of PID peaked in 2000–08 at 12·5 per 100,000 live births.

Referrals

- Patients with primary immunodeficiency. **A completed proforma must accompany all referrals**

https://www.labs.gosh.nhs.uk/media/529306/pid_panel_pre-test_proforma_2014.doc

Mutation testing can be offered to the relatives of PID patients once a disease causing mutation has been identified.

Service offered

Next generation sequencing of 82 genes (see list below) with mutation confirmation by Sanger sequencing.

List of genes included in panel

ADA, ADAM17, AICDA, AIRE, BTK, CASP10, CASP8, CD247, CD27, CD3D, CD3E, CD3G, CD40, CD40LG, CIITA , CORO1A, CYBA, CYBB, DCLRE1C, DOCK8, EPCAM, FAS, FASLG, FOXP3, GUCY2C, HPS1, HPS4, HPS6, ICOS, IKBKG, IL10, IL10RA, IL10RB, IL2RG, IL7R, ITGB2, ITK, JAK3, LIG4, LRBA, LYST, MAGT1, MYO5B, NCF1, NCF2, NCF4, NHEJ1, NRAS, ORAI1, PIK3R1, PLCG2, PNP, PRF1, PRKDC, PTPRC, RAB27A, RAG1, RAG2, RET, RFX5, RFXANK, RFXAP, RMRP, SH2D1A, SKIV2L, SLC37A4, STAT1, STAT3, STAT5A, STAT5B, STX11, STXBP2, TAP1, TAP2, TAPBP, TNFRSF13B, TTC37, UNC13D, UNG, WAS, XIAP, ZAP70

Technical

Mutation screening is carried out by next generation sequencing with library preparation using a Sure Select XT custom kit followed by sequencing on the Illumina MiSeq. Data is analysed using an in-house pipeline with all mutations confirmed by Sanger sequencing.

Target reporting time

4 months for a full mutation screen in an index case (next generation sequencing).

2 weeks for familial mutation testing.

Please contact the laboratory for urgent cases.