GRID DNA TEST FOR A PATIENT WITH:

PRIMARY IMMUNE DISORDERS (PID)

Background

There are more than 300 Primary Immunodeficiency Diseases (PID) recognized by the World Health Organization.

For PID in general about 280 genes are known to be causative, nonetheless more than 50% of the phenotypic severe immunodeficiencies cannot yet be explained. The GRID Next Generation Sequencing (NGS) test allows for the parallel sequencing of all known causal genes in DNA samples from multiple patients. Determining the genetic basis of PID in patients can aid diagnosis and risk stratification, as well as identify family members who might be at risk of developing the disease.

The current version V2.0 of the GRID NGS test contains 279 genes known to contribute to primary immune disorders, including the 2015 IUIS genes (see below - box).

Request a test if:

1. You assume a high likelihood of the condition being genetic, demonstrated by either:
   - early onset
   - other affected pedigree members*

** be mindful that genetic diseases are frequently caused by de novo mutations*

And/or your patient has a clinical diagnosis of

2. **PID:** Recurrent (and/or unusual) microbial infections suggestive of severely defective innate or cell-mediated immunity, immune dysregulation or hemophagocytic syndromes. Patients have been extensively characterised through standardised cellular immunophenotyping and functional testing for lymphocytes and myeloid cells.
   For CVID use the definition according to ESID (https://esid.org/Education/Diagnostic-Criteria-PID) .

   Or

3. **"Extreme" autoimmunity and/or autoinflammation:** Patients with aggressive autoimmune disease or autoinflammation with onset at early age. This will include patients with clinical features of immunodeficiency/chronic lymphoproliferation with autoimmunity, autoinflammation and/or recurrent episodes of unexplained fever.

DO NOT request a test if there is:

1. Low suspicion of an underlying genetic cause for the condition.
2. A genetic mutation already confirmed by an NHS laboratory.
3. A secondary immune disorder.

Please discuss with us if the patient is suffering from a blood cancer that is detectable in the blood stream.

Gene list

(Version GRID V2.0)

*= non official HGNC gene name

I. Immunodeficiencies affecting cellular and humoral immunity			
ADA	☐	ITK	☐
AK2	☐	JAK3	☐
B2M	☐	LCK	☐
BCL10	☐	LIG4	☐
CARD11	☐	LRBA	☐
CD247	☐	MAGT1	☐
CD27	☐	MALT1	☐
CD3D	☐	MAP3K14 (NIK)*	☐
CD3E	☐	NHEJ1 (Cernunnos/XLF)*	☐
CD3G	☐	PRKDC	☐
CD40	☐	PTPRC	☐
CD40LG	☐	RAG1	☐
CD8A	☐	RAG2	☐
CIITA	☐	RFX5	☐
CORO1A	☐	RFXANK	☐
CTPS1	☐	RFXAP	☐
DCLRE1C	☐	RHOH	☐
DOCK2	☐	STK4 (MST1)*	☐
DOCK8	☐	TAP1	☐
ICOS	☐	TAP2	☐
IKBKB	☐	TAPBP	☐
IL21	☐	TNFRSF4 (OX40)*	☐
IL21R	☐	TRAC	☐
IL2RG	☐	UNC119	☐
IL7R	☐	ZAP70	☐

II. CID with associated or syndromic features			
ACD	☐	POLE (POLE1)*	☐
ATM	☐	RBCK1 (HOIL1)*	☐
BLM	☐	RMRP	☐
CCBE1	☐	RNF168	☐
CHD7	☐	RTEL1	☐
DCLRE1B	☐	SEMA3E	☐
DKC1 (DKC)*	☐	SLC46A1	☐
DNMT3B	☐	SMARCAL1	☐
EPG5	☐	SPINK5	☐
FOXN1	☐	SP110	☐
IKBKG (NEMO)*	☐	STAT3	☐
MCM4	☐	STAT5B	☐
MTHFD1	☐	STIM1	☐
NFKBIA (IKBA)*	☐	TBX1	☐
NHP2 (NOLA2)*	☐	TCN2	☐
NBN (NBS1)*	☐	TERC	☐
NOP10 (NOLA3)*	☐	TERT	☐
ORAI1	☐	TINF2	☐
PARN	☐	TTC7A	☐
PGM3	☐	WAS	☐
PMS2	☐	WIPF1	☐
RNF31 (HOIP1)*	☐	ZBTB24	☐
PNP (NP)*	☐		

III. Predominantly antibody deficiencies			
AICDA	☐	MSH6	☐
BLNK	☐	MS4A1 (CD20*)	☐
BTK	☐	MOGS	☐
CARD11	☐	NFKB2	☐
CD19	☐	PIK3CD	☐
CD79A	☐	PIK3R1	☐
CD79B	☐	SART3 (p110)*	☐
CD81	☐	TCF3	☐
CR2 (CD21)*	☐	TNFRSF13B (TACI)*	☐
DKC1 (DKC)*	☐	TNFRSF13C (BAFF-R)*	☐
GATA2	☐	TNFSF12 (TWEAK)*	☐
IGKC	☐	TRNT1	☐
IGHM	☐	TTC37	☐
IGLL1	☐	UNG	☐
INO80	☐		

IV. Diseases of immune dysregulation			
ACP5	☐	LYST	☐
ADAR (ADAR1)*	☐	NFAT5	☐
AIRE	☐	PRF1	☐
AP3B1	☐	PRKCD	☐
BLOC1S6 (PLDN)*	☐	RAB27A	☐
CASP10	☐	RNASEH2A	☐
CASP8	☐	RNASEH2B	☐
CECR1 (ADA2)*	☐	RNASEH2C	☐
CTLA4	☐	SAMHD1	☐
FADD	☐	SH2D1A	☐
FASLG	☐	STAT3	☐
FOXP3	☐	STX11	☐
FAS (TNFRSF6)*	☐	STXBP2	☐
IFIH1	☐	TMEM173 (STING)*	☐
IL10	☐	TPP2	☐
IL10RA	☐	TREX1	☐
IL10RB	☐	UNC13D	☐
IL2RA	☐	XIAP	☐
ITCH	☐		

V. Congenical defects of phagocyte number, function, or both			
ACTB	☐	ITGB2	☐
CEBPE	☐	JAGN1	☐
CLPB	☐	LAMTOR2 (ROBLD3)*	☐
CSF2RA	☐	NCF1	☐
CSF3R	☐	NCF2	☐
CTSC	☐	NCF4	☐
CYBA	☐	RAC2	☐
CYBB	☐	SBDS	☐
ELANE	☐	SLC35C1	☐
FERMT3	☐	SLC37A4 (G6PT1)*	☐
FPR1	☐	TAZ	☐
G6PC3	☐	USB1 (c16orf57)*	☐
GATA2	☐	VPS13B	☐
GFI1	☐	VPS45	☐
HAX1	☐	WAS	☐

VI. Defects in intrinsic and innate immunity			
APOL1	☐	IRF8	☐
CARD9	☐	ISG15	☐
CXCR4	☐	MYD88	☐
CYBB	☐	RORC	☐
FCGR3A (CD16)*	☐	RPSA	☐
FCGR3B (CD16)*	☐	STAT1	☐
IFNGR1	☐	STAT2	☐
IFNGR2	☐	TBK1	☐
IKBKG (NEMO)*	☐	TICAM1 (TRIF)*	☐
IL12B	☐	TLR3	☐
IL12RB1	☐	TMC6 (EVER1)*	☐
IL17F	☐	TMC8 (EVER2)*	☐
IL17RA	☐	TRAF3	☐
IL17RC	☐	TRAF3IP2 (ACT1)*	☐
IRAK4	☐	TYK2	☐
IRF7	☐	UNC93B1	☐

VII. Auto-inflammatory disorders			
ADAM17	☐	NLRC4	☐
CARD14	☐	NLRP12	☐
COPA	☐	NOD2	☐
IL1RN	☐	PLCG2	☐
IL36RN	☐	PSMB8	☐
LPIN2	☐	PSTPIP1	☐
MEFV	☐	SH3BP2	☐
MVK	☐	SLC29A3	☐
NLRP3	☐	TNFRSF1A	☐

VIII. Complement deficiencies			
C1QA	☐	CD59	☐
C1QB	☐	CFB	☐
C1QC	☐	CFD	☐
C1R	☐	CFH	☐
C1S	☐	CFHR1	☐
C2	☐	CFHR2	☐
C3	☐	CFHR3	☐
C4A	☐	CFHR4	☐
C4B	☐	CFHR5	☐
C5	☐	CFI	☐
C6	☐	CFP (PFC)*	☐
C7	☐	FCN3	☐
C8A	☐	ITGAM	☐
C8B	☐	MASP2	☐
C8G	☐	SERPING1	☐
C9	☐	THBD	☐
CD46	☐		

IX. Phenocopies of PID	
CSF2RA	☐
FAS (TNFRSF6)*	☐
IL17A	☐
IL22	☐
KRAS	☐
NLRP3	☐
NRAS	☐
STAT3	☐

Additional genes	
ARPC1B	☐
F12	☐
IKZF1 (IKAROS)*	☐
LIG1	☐
MBL2	☐
MPO	☐
MRE11	☐
NFKB1	☐