NHS GRAMPIAN GENETICS & MOLECULAR PATHOLOGY LABORATORY SERVICES
REQUEST FOR PRIMARY IMMUNODEFICIENCY & PAEDIATRIC RHEUMATOLOGY TESTING

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Essential Patient Demographics (Patient label can be used)		
Forename:	Surname:	
CHI No.:	Date of Birth:	Male / Female (Circle as appropriate)
Address (**must** include postcode):		
		Postcode:
Pedigree No. (if known):	Genetics Reference No. (if known):	

Essential Referrer Details	
Referring Clinician(s):	Address for Report:
Copy to:	
Ward / Department / Practice:	
Email address:	
Telephone no.:	

Essential Sample Information		
Sample Type:	Date Taken:	Time Taken:
High Risk: YES / NO If yes, please state risk _____ ***Notify lab in advance if high risk***	Urgent analysis required: YES / NO	*DNA / Molecular Genetics only* Storage only: YES / NO
Specific test requested – clear indication of appropriate test is required		
SPIDeR SCREEN: Please tick relevant boxes on pages 2-5. PID classification according to IUIS 2017/2022 (*J Clin Immunol*., 2018 38:129–143/ *J Clin Immunol*., 2022 42(7):1508–1520)	**SINGLE GENE SCREEN**: see page 5 for details	**PREDICTIVE TEST**: please enter proband's and genetic variant details
Reason for referral & relevant clinical information:		

***CONSENT:* It is the responsibility of the referring clinician to obtain informed consent from the patient / carer for the test and for the sample to be stored for future diagnostic testing.**

Signature of referring clinician: _____ ***Print name:*** _____

	I. Immunodeficiency Affecting Cellular and Humoral Immunity	
	A. Severe Combined Immunodeficiency SCID Defined by CD3 T Cell Lymphopenia |< 300/uL	
	SCID T-B+ (CD19 normal)	
	SCID T-B+NK-	*IL2RG, JAK3*
	SCID T-B+NK+	*IL7R, CD3D, CD3E, CD247, PTPRC, CORO1A, FOXN1*
	SCID T-B- (CD19 low)	
	SCID T-B-NK-	*ADA, AK2*
	SCID T-B-NK+ w/ microcephaly	*LIG4, NHEJ1, PRKDC*
	SCID T-B-NK+ w/out microcephaly	*RAG1, RAG2, DCLRE1C (ARTEMIS)*

	II Combined Immunodeficiencies (less profound than SCIDs)	
	A. CID without associated syndromes	
	CID without associated syndromes	*B2M, BCL10, CARD11, CD3G, CD8A, CD40, CD40LG, CIITA, DOCK2, DOCK8, ICOS, IKBKB, IKZF1, IL21, IL21R, ITK, LCK, MALT1, MAP3K14, MSN, RELB, RFXANK, RFXAP, RFX5, RHOH, STK4, TAP1, TAP2, TAPBP, TFRC, OX40 (TNFRSF4), TRAC, ZAP70*
	B. Combined Immunodeficiency (CID) with Associated or Syndromic Features	
	1. Congenital thrombocytopenia	
	Wiskott Aldrich Syndrome	*WAS*
	WIP deficiency	*WIPF1*
	ARPC1B deficiency	*ARPC1B*
	2. DNA repair defects	
	Ataxia telangiectasia	***ATM***
	Nijmegen breakage syndrome	***NBS1 (NBN)***
	Bloom syndrome	***BLM***
	PMS2 deficiency	***PMS2***
	Immunodef. w/centromeric instability and facial anomalies	*DNMT3B, ZBTB24, CDCA7, HELLS*
	MCM4 deficiency	*MCM4*
	RNF168 deficiency	*RNF168*
	POLE1 deficiency	*POLE1*
	POLE2 deficiency	*POLE2*
	NSMCE3 deficiency	*NSMCE3*
	ERCC6L2 (Hebo) deficiency	*ERCC6L2*
	Ligase 1 deficiency	*LIG1*
	GINS1 deficiency	*GINS1*
	3. Immuno-osseous dysplasias	
	Cartilage Hair Hypoplasia	*RMRP*
	Schimke syndrome	*SMARCAL1*
	MYSM1 deficiency	*MYSM1*
	MOPD1 deficiency	*RNU4ATAC*
	EXTL3 deficiency	*EXTL3*
	4. Thymic defects with congenital anomalies	
	TBX deficiency	*TBX1*
	Charge syndrome	*CDH7, SEMA3E*
	FOXN1 haploinsufficiency	*FOXN1*
	5. Hyper IgE syndromes (HIES)	
	AD-HIES (Job syndrome)	*STAT3*
	Comel Netherton syndrome	*SPINK5*
	PGM3 deficiency	*PGM3*
	Loeys-Dietz syndrome	*TGFBR1*
	CARD11 deficiency	*CARD11*
	6. Defects of Vitamin B12 and folate metabolism	
	Defects of vitamin 12 and folate metabolism	*TCN2, SLC46A1, MTHFD1*
	7. Anhydrotic ectodermodysplasia with ID	
	Anhydrotic ectodermodysplasia with ID	*IKBKG (NEMO), NFKBIA (IKBA)*

8. Calcium channel defects	
Calcium channel defects	*ORAI1, STIM1*
9. Others	
Purine nucleoside phosphorylase deficiency	*PNP*
ID with multiple intestinal atresias	*TTC7A*
Hepatic veno-occlusive disease w/ immunodeficiency (VODI)	*SP110*
Vici syndrome	*EPG5*
Hennekam-lymphangiectasia-lymphedema syndrome	*CCBE1, FAT4*
STAT5B deficiency	*STAT5B*
Kabuki syndrome	*KMT2D (MLL2), KDM6A*
Tricho-Hepato-Enteric syndrome (THES)	*TTC37, SKIV2L*
BCL11B deficiency	*BCL11B*
HOIL1 deficiency	*RBCK1*
HOIP deficiency	*RNF31*
KMT2A deficiency (Wiedemann-Steiner syndrome)	*KMT2A*

III. Predominantly Antibody Deficiencies	
A. Hypogammaglobulinaemia **(IgG, IgA and/or IgM low)**	
B absent	*BTK, IGHM, CD79A, CD79B, BLNK, IGLL1, PIK3R1, TCF3*
B >1% Common variable immune deficiency phenotype	*PIK3CD, **PTEN**, CD81, TNFRSF13B (TACI), TNFRSF13C (BAFFR), TWEAK (TNFSF12), MOGS, TTC37, IRF2BP2, CD19, CD20 (MS4A1), TRNT1, NFKB1, NFKB2, IKZF1 (IKAROS), ATP6AP1*
B. Other Antibody Deficiencies	
Hyper IgM Syndromes	*AICDA, UNG, INO80, **MSH6***
Isotype, Light Chain, or Functional Deficiencies	*IGKC*
High Bc numbers due to constitutive NF-kB activation	*CARD11*

IV. Disease of Immune Dysregulation	
A. Hemophagocytic Lymphohistiocytosis HLH & EBV Susceptibility	
Hypopigmentation (HLH)	
Chediak Higashi syndrome	*LYST*
Griscelli syndrome type 2	*RAB27A*
Hermansky Pudlak syndrome type 10	*AP3B1*
Hermansky Pudlak syndrome type 2	*AP3D1*
Familial HLH Syndromes	*PRF1, UNC13D, STX11, STXBP2*
Susceptibility to EBV	
Susceptibility to EBV	*RASGRP1, CD70, CTPS1, RLTPR (CARMIL2), ITK, MAGT1, PRKCD*
EBV associated HLH	*SH2DIA, XIAP, CD27, FAAP24*
B. Syndromes with Autoimmunity and Others	
Syndromes with autoimmunity (w/ increased CD4-CD8-TCR α/β) ALPS	*TNFRSF6 (FAS), TNFSF6 (FASLG), CASP10, CASP8, FADD*
Syndromes with autoimmunity (with occasionally increased CD4-CD8-TCR α/β)	*LRBA, STAT3*
Syndromes with autoimmunity (w/out increased CD4-CD8-TCR α/β, w/out regulatory T Cell defects)	*AIRE, ITCH, ZAP70, TPP2, JAK1, PEPD*
Syndromes with autoimmunity (w/out increased CD4-CD8-TCR α/β, with regulatory T Cell defects)	*FOXP3* (IPEX), *IL2RA, CTLA4, BACH2*
Immune Dysregulation with Colitis	*IL10, IL10RA, IL10RB, NFAT5*

V. Congenital Defects of Phagocyte Number, Function, or Both	
A. Neutropenia	
Syndrome associated	
Shwachman-Diamond syndrome	*SBDS, DNAJC21*
G6PC3 deficiency	*G6PC3*
Glycogen storage disease type 1b	*G6PT1 (SLC37A4)*
Cohen syndrome	*COH1 (VPS13B)*
Barth syndrome	*TAZ*

	Clericuzio syndrome	*C16ORF57 (USB1)*
	VPS45 deficiency	*VPS45*
	P14/LAMTOR2 deficiency	*LAMTOR2*
	JAGN1 deficiency	*JAGN1*
	3-Methylglutaconic aciduria	*CLPB*
	SMARCD2 deficiency	*SMARCD2*
	WDR1 deficiency	*WDR1*
	HYOU1 deficiency	*HYOU1*
	No syndrome associated	*ELANE, HAX1, GFI1, WAS, CSF3R, MKL1 (MRTFA)*
	B. Functional Defects	
	Syndrome associated	
	Cystic fibrosis	*CFTR*
	Papillon-Lefèvre	*CTSC*
	Localized juvenile periodontitis	*FPR1*
	β-Actin	*ACTB*
	Leukocyte adhesion deficiency (LAD)	*ITGB2 (LAD I), SLC35C1 (LAD II), FERMT3 (LAD III)*
	No syndrome associated, w/ normal DHR assay/ NBT test	
	MonoMac syndrome	*GATA2*
	Specific granule deficiency	*CEBPE*
	Pulmonary alveolar proteinosis	*CSF2RA, CSF2RB*
	No syndrome associated, w/ abnormal DHR assay/ NBT test	
	Chronic granulomatous disease (CGD)	*CYBB, NCF1, CYBA, NCF4, NCF2*
	RAC 2 deficiency	*RAC2*
	G6PD deficiency Class I	*G6PD*

	VI. Defects in Intrinsic and Innate Immunity	
	A. Bacterial and Parasitic Infections	
	Predisposition to invasive bacterial infections	*IRAK4, MYD88, IRAK1, TIRAP, RPSA, HMOX1*
	Predisposition to parasitic and fungal infections	*STAT1, IL17F, 1L17RA, IL17RC, ACT1 (TRAF3IP2), CARD9, APOL1*
	Others	
	Osteopetrosis	*TNFRSF11A, PLEKHM1, TCIRG1, CLCN7, OSTM1, SNX10, TNFSF11*
	Hydradenitis suppurativa	*PSENEN, NCSTN, PSEN*
	Acute liver failure due to NBAS deficiency	*NBAS*
	Acute necrotising encephalopathy	*RANBP2*
	B. Mendelian Susceptibility to Mycobacterial Disease (MSMD) and Viral Infection	
	MSMD (severe phenotypes)	*IFNGR1, IFNGR2*
	MSMD (moderate phenotypes)	*IL12RB1, IL12B, STAT1, IFNGR1, IFNGR2, TYK2, ISG15, CYBB, IRF8, RORC, JAK1*
	Predominant susceptibility to viral infection	
	Epidermodysplasia verruciformis (HPV)	*TMC6, TMC8, CXCR4* (WHIM)
	Predominant susceptibility to viral infection – Herpes simplex Encephalitis	*TLR3, UNC93B1, TRAF3, TICAM1(TRIF), TBK1, IRF3*
	Predisposition to severe viral infection	*STAT1, STAT2, IRF7, IFNAR2, FCGR3A, IFIH1*

	VII. Auto-inflammatory Disorders	
	Monogenic Autoinflammatory Diseases (ISSAID/EMQN) * NEW	*MEFV, MVK, TNFRSF1A, NLRP3, ADA2, NOD2, PSTPIP1, TNFAIP3*
	Recurrent inflammation (Recurrent fever)	*MEFV, MVK, TNFRSF1A*
	Systemic inflammation with urticaria rash	*NLRP3, NLRP12, PLC2G, NLRP1, TNFAIP3*
	Others	*PSMB8, COPA, NLRC4*
	Sterile inflammation (predominant on the bone/ joints)	*PSTPIP1, LPIN2, IL1RN, SH3BP2*
	Sterile inflammation (predominant on the skin)	*NOD2, CARD14, IL36RN, ADAM17, SLC29A3, OTULIN, AP1S3*
	Type 1 interferonopathies	*TREX1, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, ADAR1, IFIH1, ACP5, TMEM173, CECR1 (ADA2), POLA1, USP18*

	VIII. Complement Deficiencies	
	High susceptibility to infections	
	Disseminated Neisserial infections	*C5, C6, C7, C8A, C8B, C8G, C9, PFC (CFP), CFD*
	Recurrent pyogenic infections	*C3, MASP2, FCN3, CFB*
	Low susceptibility to infections	
	SLE-like syndrome	*C1QA, C1QB, C1QC, C1R, C1S, C2, C4A, C4B*
	Low susceptibility to infection (others)	*SERPING1, CD59, CD55*

	Others	
	Very early onset inflammatory bowel disease VEO-IBD	*ADAM17, AICDA, CD40LG, BTK, CD3G, ZAP70, WAS, CYBA, CYBB, *NCF1, NCF2, NCF4, DOCK8, EPCAM (Sanger only), FOXP3, GUCY2C, HPS1, HPS4, HPS6, ADA, IL2RG, LIG4, DCLRE1C, RAG2, IL10, Il10RA, IL10RB, ITGB2, LRBA, ICOS, PIK3R1, PLCG2, RET, SH2D1A, XIAP, SKIV2L, TTC37, SLC37A4, STAT1, STAT3, STXBP2, MYO5B*
	Wiskott Aldrich syndrome	*WAS*
	Hereditary angioedema - full screen	*SERPING1, F12, ANGPT1, PLG*

	Rheumatology	
	Assoc. with GI inflammation	*ADAM17, AICDA, AP3B1, B2M, BTK, CBL, CD40LG, CORO1A, CTC1, CTPS1, CYBA, CYBB, DCLRE1C, DOCK8, FERMT1, FOXP3, GUCY2C, HPS1, HPS4, HPS6, ICOS, IFNGR1, IFNGR2, IKBKG, IL10RA, IL2RA, ITGB2, MAGT1, NCF1, NCF2, NCF4, NF1, PIK3CD, PIK3R1, PTEN, PYCARD, SKIV2L, SLC37A4, STK4, TTC37, VPS13B, WAS*
	Hereditary amyloidosis	*APOA1, APOA2, APOA4, APOC2, APOC3, APOE, FGA, GSN, IL31RA, LYZ, TTR, UNC13D*
	HLH	*DNASE2, LYST, PRF1, RAB27A, SLC29A3, XIAP*
	Interferonopathy / SLS / AGS / complement	*ACP5, ADAM17, C1QA, C1QB, C1QC, C1R, C2, C3, C5, C6, C7, C8A, C8B, C9, CFH, CFHR5, CFI, CFP, DNASE1, DNASE1L3, IFIH1, IRF8, RASGRP1, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, SNORD118, TREX1, USP18*
	Misc. Autoinflammatory conditions	*ADA2, AIRE, AP1S3, CASP10, CASP8, COPA, COL7A1, CPT2, FAS, FASLG, FLNA, HTR1A, IL10, IL10RB, IL12B, IL12RB1, IL1RN, IL36RN, ISG15, LACC1, LPIN2, LRBA, LYN, MASP2, MAT2A, MBL2, MEFV, MVK, MYD88, NLRC4, NLRP1, NLRP12, NLRP3, NLRP6, NLRP7, NOD2, NRAS, OTULIN, PRKCD, PLCG2, POMP, PRG4, PSMA3, PSMB4, PSMB8, PSMB9, PSTPIP1, RAG1, RANBP2, SCN9A, SERPING1, SH2D1A, SH3BP2, TMEM173, TNFAIP3, TNFRSF11A, TNFRSF1A, TRAP1, TRNT1, USB1, WDR1*
	Stroke	*CBS, CST3, GLA, HTRA1, NOTCH3, ADA2*
	Vasculopathy	*ACTA2, BMPR2, COL3A1, COL4A1, COL5A1, COL5A2, EFEMP2, ELN, FBN1, FBN2, FOXE3, GUCA1B, LMNA, LOX, MFAP5, MYH11, MYLK, NOTCH1, PLOD1, PRKG1, RHOD, RNF213, SKI, SLC2A10, SMAD2, SMAD3, SMAD4, STX11, STXBP2, TGFB2, TGFB3, TGFBI, TGFBR1, YY1AP1*

	Single gene screens	
	C1 INH deficiency - HAE Type I+II	*SERPING1* only - Sanger screen + MLPA
	X-linked CGD	*CYBB* Sanger screen + MLPA
	Familial HLH due to *PRF1* variants	*PRF1* Sanger screen + MLPA
	Adenosine deaminase deficiency (DADA) *NEW	*ADA2* Sanger screen + MLPA *(CECR1)*

Please note, gene panels highlighted in BOLD RED containing genes associated with hereditary cancers (MSH6, EPCAM, ATM, NBS/NBN, PMS2, BLM, PTEN) require additional consent

Incomplete or illegible referral forms may lead to sample rejection and a delay in testing
Please see www.nhsgrampian.org/medicalgenetics for sample & transport requirements