Next Generation Sequencing Services

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Testing Workflow

Library Preparation

SureSelect/Illumina lab work performed in Sheffield up until August 2022

- Shearing of genomic DNA using the Covaris E220 sonicator.
- End repair, A tailing and ligation of adaptors using SureSelectXT library system (Agilent Technologies).
- Enrichment by SureSelect target enrichment (Agilent Technologies) using custom in house designed probes. Samples have barcode tags added following target enrichment.
- Sequencing on the Illumina HiSeq (or from Nov 2021 on Illumina MiSeq) using the HiSeq Rapid SBS Kit v2 performing 2 x 108 bp paired end reads

SureSelect/Illumina lab work performed in Leeds (Central NEY GLH lab)

- Shearing of genomic DNA using the Covaris E220 sonicator.
- End repair, A tailing and ligation of adaptors using SureSelectXT library system (Agilent Technologies). SureSelectXT HS2 implemented in December 2022.
- Enrichment by SureSelect target enrichment (Agilent Technologies) using custom in house designed probes. Samples have barcode tags added following target enrichment.
- Sequencing on the Illumina NextSeq using the NextSeq 500/550 High Output Kit v2.5 (300 Cycles), performing paired 150bp reads.

AmpliSeq/Ion Torrent

- Generate amplicon libraries using Ion AmpliSeq (Thermo Fisher Scientific) primer pools, and add patient specific barcodes.
- Ion Chef System provides automated, high-throughput preparation of template-positive Ion Sphere Particles (ISPs) and Ion 520, 530 or 540 chip loading.
- Sequencing on the Ion S5 or S5 Prime system.

Data Analysis

- Based on the open source 'Best Practices' workflow by the Broad Institute (for additional information, see http://www.broadinstitute.org/gatk/guide/best-practices).
- BWA alignment of reads to human genome build hg19 (build 37).
- Generation of depth of coverage reports. Checked using Alamut Visual (Interactive Biosoftware).
- For SureSelect/Illumina: a minimum threshold of 30-fold read depth is set for exonic sequences and intronic sequences up to and including 5 bp from exon. A minimum threshold of 18-fold read depth is set for intronic sequences from 6 bp to 25 bp from exon. For AmpliSeq/Ion Torrent minimum 50x for exonic regions and ±5bp into introns and minimum 30x for intronic regions between 6 and 25bp from exons.
- Identification of variants using HaplotypeCaller. Annotation from dbSNP and COSMIC (currently dbSNP150 and COSMIC v67 but updated with new releases)
- Variants filtered against in-house polymorphism lists and Best Practice Guidelines for the evaluation of pathogenicity and the reporting of sequence variants in clinical molecular genetics (Association for Clinical Genetic Science).
- Assessment of copy number variants using DeCON software for SureSelect/Illumina data generated in Sheffield. This analysis can detect single-exon deletions, with smallest deletion detected 116bp (largest = 200kbp). With thresholds in place, at exon-level resolution, non-mosaic CNVs sensitivity 1.0 and specificity 0.989.
- Assessment of copy number variants using comparative depth read analysis for SureSelect/Illumina data generated in Leeds (Central NEY GLH lab), includes analysis of single exon deletions and duplications (smallest deletion = 43bp) with sensitivity 100%.
- Note copy number variants are not currently analysed using AmpliSeq/Ion Torrent platform

SureSelect/Illumina lab work performed in Leeds (Central NEY GLH lab)

- Samples are analysed using varDB, a tool for filtering variants designed, built, and maintained by Leeds Genetics Laboratory as part of the NEY GLH.
- Genes and transcripts of interest are applied to each Sample. Variants are filtered using the following criteria against annotations derived from Alamut Batch v1.9 (database version 2018-01-18):
  - In a Gene associated with the Sample.
  - In a Transcript associated with the Sample.

  - Does not have an artefact signature (relative to locally sequenced population).
  - Has a HGMD classification of DM or DM? (irrespective of population frequency)
  - Has an ExAC All or gnomAD All frequency less than 0.06.
  - For synonymous variants:
    - distNearestSS between -3 and 3
    - nearestSSChange less than -0.1
    - localSS_varMaxEntScore greater than 4.0
  - For intronic variants:
    - nearestSSChange less than -0.1
    - localSS_varMaxEntScore greater than 4.0
- Individual variant calls which pass filtering are then investigated further to check whether they are genuine variant calls.
- Genuine variant calls are then classified by Clinical Scientists according to the ACMG Variant Classification guidelines.

Haemato Oncology – see relevant section at end of document

Post analysis

- Confirmation of clinically significant sequence variants by Sanger sequencing and/or MLPA (or ddPCR) as necessary (see below).
- Filling of gaps with low depth of coverage by Sanger sequencing as necessary. Gaps that fall within genes that have an individual whole gene sequencing service listed on the UKGTN service website as filled. The locations of all gaps that are not filled by Sanger sequencing are clearly indicated on the report.
- Creation of a diagnostic report combining clonal and Sanger sequence data that includes clinical interpretation of all the variants identified that are clearly pathogenic, likely to be pathogenic or variants of uncertain significance with high probability of pathogenicity (see ACGS variant interpretation guidelines 2020).

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Gene panel content

Our NGS panels are updated according to the national test directory updates (April and October) and the gene content aligns with designated green genes on NHS PanelApp: https://nhsgms-panelapp.genomicsengland.co.uk/. For some panels, amber genes are also included in the design but are not routinely analysed. As amendments to the panels require a custom SureSelect redesign and validation there can be delays to implementation of new genes and/or panels after the test directory updates. NHSE is kept aware of any delays. The tested gene list is included in the report footer. The NHS version of PanelAPP for green genes is used by the laboratories but there are current delays for NHS PanelApp website updates.

Confirmation of variants detected by NGS

A risk assessment was carried out in June 2016 regarding the necessity for confirming variants identified by NGS using orthogonal technology (typically Sanger sequencing). The risk assessment was based on best practice guidelines, analysis of the quality of NGS data produced and the robustness of the tube transfer checking process within the laboratory.

The conclusion was: -

SDGS will no longer performs confirmation of single nucleotide substitution variants rated as class 3, 4 and 5, with a QUAL score of ≥3000 (and depth of coverage of ≥30x [≥18x for -25_-6 and +6_+25]), detected by SureSelect NGS workflows run on the MiSeq and HiSeq2500 platforms, and AmpliSeq/Ion Torrent workflows run of S5 and S5 Prime platforms.

Exclusions to this include: -

- Indel variants - these are confirmed by Sanger sequencing, regardless of their QUAL score.
- Rare genes with highly homologous pseudogenes
- Somatic cancer panels

Copy number variants detected by analysis of NGS data (Sheffield and Leeds) must be manually inspected for presence of breakpoints. If visible breakpoints AND read depth analysis confirm a deletion or duplication, the CNV can be reported without further confirmatory testing. If breakpoints are not visible, the CNV must be confirmed by an alternative method (usually MLPA or ddPCR) before clinical reporting.

Next Generation Sequencing Panels

Familial Hypercholesterolemia panel

(wet work in Leeds Central NEY GLH lab – FH panel or temporarily outsourced to GenInCode from March 2023)

Condition	Gene
Familial hypercholesterolaemia	LDLR
Autosomal dominant type B hypercholesterolaemia	APOB
Hyperlipoproteinemia, type III	APOE
Familial hypercholesterolaemia 3	PCSK9
Autosomal recessive hypercholesterolaemia	LDLRAP1

Musculoskeletal Service

Ehlers Danlos Syndromes (R101) as PanelApp panel: Ehlers Danlos syndromes (Version 2.3) (SureSelect Design ID 3278641). wet work in Leeds Central NEY GLH lab

ADAMTS2	*BGN*	*COL3A1*	*ELN*	*PLOD1*	*SMAD3*
AEBP1	*C1R*	*COL5A1*	*FBLN5*	*PRDM5*	*TGFB2*
ALDH18A1	*C1S*	*COL5A2*	*FBN1*	*PYCR1*	*TGFB3*
ATP6V0A2	*CBS*	*COL6A1*	*FBN2*	*RIN2*	*TGFBR1*
ATP6V1A	*CHST14*	*COL6A2*	*FKBP14*	*ROBO3*	*TGFBR2*
ATP7A	*COL12A1*	*COL6A3*	*GORAB*	*SKI*	*TNXB*
B3GALT6	*COL1A1*	*DSE*	*LOX*	*SLC39A13*	*ZNF469*
B4GALT7	*COL1A2*	*EFEMP2*	*LTBP4*	*SMAD2*	

Osteogenesis Imperfecta (R102) as PanelApp panel: Osteogenesis Imperfecta (Version 3.0) (SureSelect Design ID 3278641). wet work in Leeds Central NEY GLH lab

ALPL	*CRTAP*	*P3H1*	*SP7*
B3GALT6	*DSPP*	*P4HB*	*SPARC*
B4GALT7	*FKBP10*	*PLOD2*	*TAPT1*
BMP1	*GORAB*	*PLS3*	*TENT5A (FAM46A)*
CASR	*IFITM5*	*PPIB*	*TMEM38B*
COL1A1	*LRP5*	*SEC24D*	*TRPV6*
COL1A2	*NBAS*	*SERPINF1*	
CREB3L1	*NOTCH2*	*SERPINH1*	

Multiple Exotoses (R390) (Design ID WG_IAD186831_improve.20191114). Wet work in Sheffield on S5

EXT1	*EXT2*

Thanatophoric Dysplasia (R25) (Design ID WG_IAD186831_improve.20191114)

FGFR3

Hypophosphatasia (Design ID WG_IAD186831_improve.20191114)

ALPL

Hereditary Cancer Panels

R208: Breast & Ovarian cancer (wet work in Leeds Central NEY GLH lab – Breast Ovarian Bowel BOB panel)

BRCA1	*PALB2*	*ATM*	*RAD51D*
BRCA2	*CHEK2*	*RAD51C*	*(TP53)**

*optional – only add for cases with breast cancer aged 30 or under

R207: Ovarian cancer (wet work in Leeds Central NEY GLH lab – Breast Ovarian Bowel BOB panel)

BRCA1	*BRIP1*	*MLH1*	*EPCAM* (dosage only)
BRCA2	*RAD51C*	*MSH2*	
PALB2	*RAD51D*	*MSH6*	

R210: Lynch syndrome (MMR deficiency – previously known as HNPCC) (wet work in Leeds Central NEY GLH lab – Breast Ovarian Bowel BOB panel)

MLH1	*MSH6*	*EPCAM* (dosage only)	
MSH2	*PMS2*		

R211: Inherited Polyposis and early-onset colorectal cancer (wet work in Leeds Central NEY GLH lab – Breast Ovarian Bowel BOB panel)

APC	*MLH1*	*NTHL1*	*PTEN*
BMPR1A	*MSH2*	*PMS2*	*SMAD4*
EPCAM (dosage only)	*MSH6*	*POLD1*	*STK11*
GREM1 (dosage only)	*MUTYH*	*POLE*	*RNF43*

R414: APC Associated Polyposis (wet work in Leeds Central NEY GLH lab – Breast Ovarian Bowel BOB panel)

APC			

XR224: Renal Cancer gene Panel

non-NHS patients only (Leeds Cancer reagent) wetwork in Leeds

BAP1	*FLCN*	*SDHB*	
FH	*MET*	*VHL*	

Neurogenetic Disorders

Adult onset hereditary spastic paraparesis (R60) as PanelApp panel: Hereditary spastic paraplegia - adult onset (Version 2.0) (SureSelect Design ID: 3414601).

ABCD1	*CAPN1*	*GBE1*	*PSEN1*
ADAR	*CPT1C*	*GCH1*	*REEP1*
ALDH18A1	*CYP27A1*	*GJA1*	*RTN2*
AP4B1	*CYP7B1*	*KCNA2*	*SACS*
AP4E1	*DARS1*	*KIF1A*	*SLC25A15*
AP4M1	*DDHD1*	*KIF1C*	*SPAST*
AP4S1	*DDHD2*	*KIF5A*	*SPG11*
AP5Z1	*ERLIN2*	*NIPA1*	*SPG21*
ATL1	*FA2H*	*OPA3*	*SPG7*
ATP13A2	*FBXO7*	*PCYT2*	*TUBB4A*
B4GALNT1	*FXN*	*PLP1*	*UBAP1*
BSCL2	*GALC*	*PNPLA6*	*WASHC5*
C19orf12	*GBA2*	*POLR3A*	*ZFYVE26*

Childhood onset hereditary spastic paraplegia (R61) as PanelApp panel: Hereditary spastic paraplegia - childhood onset (Version 3.0) (SureSelect Design ID: 3414601).

ABCD1	ATP13A2	ENTPD1	HPDL	PLP1	SPAST
ADAR	B4GALNT1	ERLIN1	IFIH1	PNPLA6	SPG11
AFG3L2	BCAS3	ERLIN2	KCNA2	POLR3A	SPG21
AIMP1	BSCL2	FA2H	KDM5C	REEP1	SPG7
ALDH18A1	MTRFR	FAR1	KIDINS220	REEP2	STN1
ALDH3A2	C19orf12	FARS2	KIF1A	RNASEH2B	TFG
ALS2	CAPN1	FXN	KIF1C	RNU7-1	TUBB4A
AP4B1	CPT1C	GALC	KIF5A	RTN2	UBAP1
AP4E1	CYP27A1	GBA2	L1CAM	SACS	UCHL1
AP4M1	CYP2U1	GCH1	MAPK8IP3	SERAC1	WASHC5
AP4S1	CYP7B1	GJA1	NIPA1	SLC16A2	WDR45B
AP5Z1	DARS1	GLRX5	NKX6-2	SLC1A4	ZFYVE26
ARG1	DDHD1	GPT2	NT5C2	SLC25A15	
ARL6IP1	DDHD2	HACE1	OPA3	SLC2A1	
ATL1	ELOVL1	HIKESHI	PCYT2	SPART	

Adult onset Neurodegenerative Disorders (R58) as PanelApp panel: Hereditary spastic paraplegia - childhood onset (Version 3.0) (SureSelect Design ID: 3414601).

ABCD1	CHCHD2	EIF2B1	HEXB	OPTN	SNCA	VPS13A
AFG3L2	CHMP2B	EIF2B2	HNRNPA1	PANK2	SOD1	VPS35

ALS2	CLCN2	EIF2B3	HTRA1	PARK7	SPAST	WDR45
ANG	CLN6	EIF2B4	ITM2B	PDGFB	SPG11	XPR1
ANXA11	COASY	EIF2B5	KCNC3	PDGFRB	SQSTM1	
APP	CP	ELOVL4	KCND3	PFN1	SYNJ1	
ARSA	CSF1R	EPM2A	KIAA1161	PINK1	TARDBP	
ATP13A2	CTSF	ERBB4	KIF5A	PLA2G6	TBK1	
ATP1A3	CYP27A1	FBXO7	LRRK2	PRKN	TMEM240	
ATP7B	CYP7B1	FTL	LYST	PRNP	TREM2	
AUH	DARS2	FUS	MAPT	PSEN1	TTC19	
C19orf12	DCTN1	GCH1	NHLRC1	PSEN2	TYROBP	
CACNA1G	DNAJC5	GFAP	NOTCH3	RNF216	UBQLN2	
CCNF	DNAJC6	GRN	NPC1	SETX	VAPB	
CHCHD10	DNMT1	HEXA	NPC2	SLC20A2	VCP	

Adult onset dystonia, chorea or related movement disorder (R56) as PanelApp panel: Adult onset movement disorder (Version 2.0) (SureSelect Design ID: 3414611)

ACTB	DCAF17	LYST	PRRT2	TOR1A
AFG3L2	DCTN1	MAPT	RAB39B	TUBB4A
ANO3	DNAJC6	NKX2-1	RNF216	VPS13A
APTX	FBXO7	PANK2	SGCE	VPS16
ATM	FTL	PARK7	SLC19A3	VPS35
ATP13A2	GBA	PDE10A	SLC20A2	WDR45
ATP1A2	GCH1	PDGFB	SLC2A1	
ATP1A3	GFAP	PDGFRB	SLC30A10	
ATP7B	GNAL	PINK1	SNCA	
C19orf12	GRN	PLA2G6	SPG11	
CACNA1A	GTPBP2	PNKD	SPR	
CHMP2B	HPCA	PPP2R5D	SYNJ1	
CP	KIAA1161	PRKN	TBK1	
CSF1R	KMT2B	PRKRA	THAP1	
CYP27A1	LRRK2	PRNP	TIMM8A	

Childhood onset dystonia, chorea or related movement disorder (R57) as PanelApp panel: Childhood onset dystonia or chorea or related movement disorder (Version 2.0) (SureSelect Design ID: 3414611)

ABAT	COASY	GLRA1	MARS2	PDE2A	SGCE	VAMP2
ACOX1	COX10	GLRB	MECR	PDGFB	SLC16A2	VPS13A

ACTB	COX15	GM2A	MED27	PDHA1	SLC19A3	VPS13D
ADAR	CSTB	GNAL	MRE11	PDHX	SLC20A2	VPS16
ADCY5	DCAF17	GNAO1	MTFMT	PET100	SLC2A1	VPS41
AFG3L2	DDC	GNB1	NDUFA1	PINK1	SLC30A10	VPS4A
ALDH18A1	DHDDS	GRIN1	NDUFA10	PLA2G6	SLC39A14	WDR45
ANO3	DLAT	GTPBP2	NDUFA2	PNKD	SLC6A3	WDR73
AP1S2	DLD	HCFC1	NDUFAF5	PNKP	SLC6A8	YIF1B
APTX	DNAJC12	HEXA	NDUFAF6	POLR3A	SPR	YY1
ARSA	ECHS1	HIBCH	NDUFS1	PRKN	SUCLA2	ZSWIM6
ATM	EIF2AK2	HNRNPH1	NDUFS4	PRKRA	SUOX	
ATP13A2	FA2H	HPCA	NDUFS7	PRNP	SURF1	
ATP1A2	FBXO7	HPRT1	NDUFS8	PRRT2	SYNJ1	
ATP1A3	FITM2	HSPD1	NDUFV1	PTS	TAF1	
ATP7B	FOLR1	HTRA2	NGLY1	QDPR	TARS2	
BCAP31	FOXG1	IFIH1	NKX2-1	RAB39B	TH	
BCS1L	FOXRED1	IMPDH2	NKX6-2	RNASEH2B	THAP1	
C19orf12	FTL	IRF2BPL	NPC1	RNASEH2C	TIMM8A	
CACNA1A	FUCA1	KCNA1	NPC2	RNASET2	TOR1A	
CACNA1G	FXN	KCNMA1	OCLN	RNU7-1	TPK1	
CACNB4	GBA	KCNQ2	OPA3	SAMHD1	TREX1	
CAMK4	GCDH	KCTD17	PANK2	SCN1A	TUBB4A	
CLN3	GCH1	KIF1C	PCCA	SCN8A	UBTF	
CLN5	GJC2	KMT2B	PCCB	SERAC1	VAC14	
CLPB	GLB1	LRPPRC	PDE10A	SETX	VAMP1	

Paroxysmal central nervous system disorders (R66) as PanelApp panel: Paroxysmal central nervous system disorders (Version 2.0) (SureSelect Design ID: 3414611)

ADCY5	*KCNQ2*
ATAD1	*PDE10A*
ATP1A2	*PNKD*
ATP1A3	*PRRT2*
CACNA1A	*SCN1A*
DNMT1	*SLC1A3*
GLRA1	*SLC2A1*
GLRB	*SLC6A5*
KCNA1	*VAMP2*
KCNMA1	

Acute Rhabdomyolysis (R419) as PanelApp panel: Acute Rhabdomyolysis (Version 1.0) (SureSelect Design ID: 3427441)

ACAD9	*DYSF*	*ISCU*	*SCN4A*
ACADM	*ENO3*	*LAMP2*	*SGCA*

ACADVL	*ETFA*	*LDHA*	*SIL1*
AGL	*ETFB*	*LPIN1*	*SLC22A5*
ALDOA	*ETFDH*	*OBSCN*	*TANGO2*
AMPD1	*FDX2*	*PFKM*	*TK2*
ANO5	*FKRP*	*PGAM2*	
CACNA1S	*FLAD1*	*PGK1*	
CAV3	*GAA*	*PGM1*	
CHKB	*GBE1*	*PHKA1*	
COQ4	*GMPPB*	*PHKB*	
COQ8A	*GYG1*	*POLG*	
CPT2	*GYS1*	*POLG2*	
DGUOK	*HADHA*	*PYGM*	
DMD	*HADHB*	*RYR1*	

Hereditary ataxia with onset in adulthood (R54) as PanelApp panel: Hereditary ataxia - adult onset (Version 3.0) (SureSelect Design ID: 3427441)

AAAS	*COASY*	*FGF14*	*MFN2*	*PRNP*	*SQSTM1*	*WWOX*
ABHD12	*COG5*	*FLVCR1*	*MMACHC*	*PRRT2*	*SRD5A3*	*ZFYVE26*
ADCY5	*COQ8A*	*FOLR1*	*MRE11*	*PTRH2*	*STUB1*	
AFG3L2	*COX20*	*FXN*	*MSTO1*	*PUM1*	*SYNE1*	
ANO10	*CP*	*GBA2*	*MTTP*	*RARS2*	*SYNGAP1*	
APTX	*CSTB*	*GFAP*	*NHLRC1*	*RNF170*	*TERT*	
ARMC9	*CWF19L1*	*GJC2*	*NKX2-1*	*RNF216*	*TMEM240*	
ARSA	*CYP27A1*	*GLRA1*	*NKX6-2*	*ROBO3*	*TOE1*	
ATCAY	*CYP2U1*	*GLRB*	*NPC1*	*SACS*	*TPP1*	
ATM	*DARS2*	*GOSR2*	*NPC2*	*SAMD9L*	*TSEN2*	
ATP1A2	*DDHD2*	*GPAA1*	*OPA1*	*SCN1A*	*TSEN54*	
ATP1A3	*DNAJC19*	*GRID2*	*OPA3*	*SCN8A*	*TTBK2*	
ATP7B	*DNAJC5*	*GRM1*	*OPHN1*	*SEPSECS*	*TTPA*	
AUH	*DNMT1*	*HEXA*	*PACS2*	*SETX*	*TUBA1A*	
B3GALNT2	*EIF2B1*	*HEXB*	*PEX16*	*SIL1*	*TUBB2B*	
BRF1	*EIF2B2*	*IRF2BPL*	*PEX6*	*SLC1A3*	*TUBB3*	
CA8	*EIF2B3*	*ITPR1*	*PLA2G6*	*SLC25A46*	*TUBB4A*	
CACNA1A	*EIF2B4*	*KCNA1*	*PMPCA*	*SLC2A1*	*TWNK*	
CACNA1G	*EIF2B5*	*KCNA2*	*PMPCB*	*SLC39A8*	*UBA5*	
CAMTA1	*ELOVL4*	*KCNC3*	*PNKD*	*SLC52A2*	*VLDLR*	
CAPN1	*EPM2A*	*KCND3*	*PNKP*	*SLC9A6*	*VPS13D*	
CASK	*ERCC4*	*KCNJ10*	*PNPLA6*	*SNX14*	*VPS53*	
CLCN2	*EXOSC3*	*KCNQ2*	*POLG*	*SPG7*	*WDR73*	
CLN6	*EXOSC8*	*KIF1C*	*POLR3A*	*SPR*	*WDR81*	
COA7	*EXOSC9*	*MARS2*	*PRKCG*	*SPTBN2*	*WFS1*	

Hereditary ataxia with onset in childhood (R55) as PanelApp panel: Ataxia and cerebellar anomalies - narrow panel (Version 3.0) (SureSelect Design ID: 3427441)

AAAS	*CLCN2*	*ELOVL4*	*ITPR1*	*PDYN*	*ROBO3*	*TPP1*
ABCB7	*CLN6*	*EPM2A*	*KCNA1*	*PEX16*	*SACS*	*TSEN2*
ABHD12	*COQ8A*	*EXOSC3*	*KCNC3*	*PLA2G6*	*SAR1B*	*TSEN34*
ADGRG1	*COX20*	*FGF14*	*KCND3*	*PMPCA*	*SEPSECS*	*TSEN54*
AFG3L2	*CP*	*FKRP*	*KCNJ10*	*PNKP*	*SETX*	*TTBK2*
AMPD2	*CTBP1*	*FKTN*	*KIF1C*	*PNPLA6*	*SIL1*	*TTC19*
ANO10	*CWF19L1*	*FLVCR1*	*LARGE1*	*POLG*	*SLC1A3*	*TTPA*
AP1S2	*CYP27A1*	*FOLR1*	*LARS2*	*POLR3A*	*SLC2A1*	*TUBA1A*
APTX	*CYP2U1*	*FXN*	*MARS2*	*POMGNT1*	*SLC9A6*	*TUBB2B*
ARSA	*DARS2*	*GBA2*	*MMACHC*	*POMGNT2*	*SNX14*	*TUBB3*
ATCAY	*DDHD2*	*GFAP*	*MORC2*	*POMT1*	*SPG7*	*TUBB4A*
ATM	*DKC1*	*GJC2*	*MRE11*	*POMT2*	*SPTBN2*	*TWNK*
ATP1A3	*DNAJC19*	*GMPPB*	*MTTP*	*PRKCG*	*SRD5A3*	*VLDLR*
B3GALNT2	*DNAJC5*	*GOSR2*	*NHLRC1*	*PRNP*	*STUB1*	*VPS13D*
CA8	*DNMT1*	*GPAA1*	*NKX6-2*	*PRRT2*	*SYNE1*	*VPS41*
CACNA1A	*EIF2B1*	*GRID2*	*NPC1*	*PTF1A*	*TGM6*	*VRK1*
CACNA1G	*EIF2B2*	*GRM1*	*NPC2*	*RARS2*	*TINF2*	*WDR73*
CAMTA1	*EIF2B3*	*HEXA*	*OPA3*	*RELN*	*TMEM240*	*WDR81*
CASK	*EIF2B4*	*HEXB*	*OPHN1*	*RNF170*	*TMEM5*	*WFS1*
CHMP1A	*EIF2B5*	*ISPD*	*PAX6*	*RNF216*	*TOE1*	*WWOX*

Haematology disorders

Haems mini-panel

(Ampliseq Design ID: IAD162775_197) Wetwork in Sheffield

F2	*VKORC1*	*CSF3R*	*HAMP*
F8	*F7*	*GATA2*	*TFR2*
F9	*F10*	*RUNX1*	*SLC40A1*
F11	*GGCX*	*CEBPA*	*LMAN1*
GP1BA	*F5*	*ANKRD26*	*MCFD2*
GP1BB	*ADAMTS13*	*DDX41*	*ITGA2B*
GP9	*VWF*	*SRP72*	*ITGB3*
MPL	*F13A1*	*HFE*	*FGA*
PROC	*F13B*	*ELANE*	*FGB*
PROS1	*NBN*	*PAX5*	*FGG*
SERPINC1	*ETV6*	*HFE2 (HJV)*	

R90.1 :: Bleeding and Platelet Disorders (Version 1.2)
https://panelapp.genomicsengland.co.uk/panels/545/
Agilent SureSelect Reagent Design ID: S3405002 – Laboratory work in YNEGLH Central Lab

ABCG5	*F13A1*	*HOXA11*	*PLAU*
ABCG8	*F13B*	*HPS1*	*PRKACG*
ACTB	*F2*	*HPS3*	*RASGRP2*
ACTN1	*F5*	*HPS4*	*RBM8A*
ACVRL1	*F7*	*HPS5*	*RUNX1*
ADAMTS13	*F8*	*HPS6*	*SERPINE1*
ANKRD26	*F9*	*ITGA2B*	*SERPINF2*
ANO6	*FERMT3*	*ITGB3*	*SLFN14*
AP3B1	*FGA*	*KDSR*	*SRC*
AP3D1	*FGB*	*KLKB1*	*STIM1*
ARPC1B	*FGG*	*KNG1*	*STXBP2*
BLOC1S3	*FLI1*	*LMAN1*	*TBXA2R*
BLOC1S6	*FYB1*	*LYST*	*TBXAS1*
CDC42	*GATA1*	*MCFD2*	*THBD*
CYCS	*GBA*	*MECOM*	*THPO*
DIAPH1	*GFI1B*	*MPIG6B*	*TPM4*
DTNBP1	*GGCX*	*MPL*	*TUBB1*
ENG	*GNE*	*MYH9*	*VIPAS39*
ETV6	*GP1BA*	*NBEA*	*VKORC1*
F10	*GP1BB*	*NBEAL2*	*VPS33B*
F11	*GP6*	*P2RY12*	*VWF*
F12	*GP9*	*PLA2G4A*	*WAS*

R91.1 :: Cytopenia NOT Fanconi Anaemia (Version 1.29)
https://panelapp.genomicsengland.co.uk/panels/519/
Agilent SureSelect Reagent Design ID: S3405002 – Laboratory work in YNEGLH Central Lab

ACD	*GATA1*	*RPL27*	*SBDS*
ADA2	*GATA2*	*RPL31*	*SRC*
ANKRD26	*GFI1*	*RPL35A*	*TAZ*
CSF3R	*HAX1*	*RPL5*	*TERC*
CTC1	*JAGN1*	*RPL9*	*TERT*
CXCR4	*KIF23*	*RPS10*	*THPO*
CYCS	*KLF1*	*RPS17*	*TINF2*
DKC1	*MECOM*	*RPS19*	*USB1*
DNAJC21	*MPL*	*RPS24*	*VPS45*
ELANE	*PARN*	*RPS26*	*WAS*
ERCC6L2	*RMRP*	*RPS29*	*WIPF1*
ETV6	*RPL11*	*RPS7*	*WRAP53*
FYB1	*RPL15*	*RTEL1*	
G6PC3	*RPL26*	*SAMD9*	

R92.1 :: Rare Anaemia (Version 1.2)
https://panelapp.genomicsengland.co.uk/panels/518/
Agilent SureSelect Reagent Design ID: S3405002 – Laboratory work in YNEGLH Central Lab

ABCB7	*GATA1*	*NT5C3A*	*RPS29*
ABCG5	*GCLC*	*PFKM*	*RPS7*
ABCG8	*GLRX5*	*PIEZO1*	*SBDS*
ADA2	*GPI*	*PKLR*	*SEC23B*
AK1	*GSR*	*PUS1*	*SLC11A2*
ALAS2	*GSS*	*RHAG*	*SLC19A2*
ALDOA	*HBA1*	*RPL11*	*SLC25A38*
AMN	*HBA2*	*RPL15*	*SLC2A1*
ANK1	*HBB*	*RPL26*	*SLC4A1*
C15orf41	*HBD*	*RPL27*	*SPTA1*
CBLIF (GIF)	*HBG1*	*RPL31*	*SPTB*
CD59	*HBG2*	*RPL35A*	*TCN2*
CDAN1	*HK1*	*RPL5*	*TF*
COX4I2	*HSPA9*	*RPL9*	*TMPRSS6*
CUBN	*KCNN4*	*RPS10*	*TPI1*
CYB5R3	*KIF23*	*RPS17*	*TRNT1*
DHFR	*KLF1*	*RPS19*	*UMPS*
EPB41	*LPIN2*	*RPS24*	*XK*
EPB42	*MTR*	*RPS26*	*YARS2*
G6PD	*MTRR*	*RPS27*	

R96.1 :: Iron Metabolism Disorders NOT common HFE mutations (Version 1.2)

https://panelapp.genomicsengland.co.uk/panels/515/

Agilent SureSelect Reagent Design ID: S3405002 – Laboratory work in YNEGLH Central Lab

ABCB7	*CYBRD1*	*HFE*	*TF*
ALAS2	*FTL*	*HJV (HFE2)*	*TFR2*
ATP7B	*GBA*	*SLC11A2*	*TMPRSS6*
BMP6	*GLRX5*	*SLC25A38*	
CP	*HAMP*	*SLC40A1*	

R97.1 :: Thrombophilia with a likely monogenic cause (Version 1.4)

https://panelapp.genomicsengland.co.uk/panels/516/

Agilent SureSelect Reagent Design ID: S3405002 – Laboratory work in YNEGLH Central Lab

ADAMTS13	*FGB*	*PLG*	*SERPIND1*
F2	*FGG*	*PROC*	*SERPINE1*
F5	*HRG*	*PROS1*	*THBD*
FGA	*PIGA*	*SERPINC1*	

R124.1:: Combined factor V and VIII deficiency (Version 1.2)

https://panelapp.genomicsengland.co.uk/panels/517/

Agilent SureSelect Reagent Design ID: S3405002 – Laboratory work in YNEGLH Central Lab

LMAN1	MCFD2

R229 :: Confirmed Fanconi or Bloom Syndrome (Version 1.7)
https://panelapp.genomicsengland.co.uk/panels/508/
Agilent SureSelect Reagent Design ID: S3405002 – Laboratory work in YNEGLH Central Lab

BLM	*FANCA*	*FANCF*	*SLX4*
BRCA1	*FANCB*	*FANCG*	*TOP3A*
BRCA2	*FANCC*	*FANCI*	*UBE2T*
BRIP1	*FANCD2*	*FANCL*	
ERCC4	*FANCE*	*PALB2*	

R405.1 :: Hereditary Erythrocytosis (Version 1.19)
https://panelapp.genomicsengland.co.uk/panels/157/
Agilent SureSelect Reagent Design ID: S3405002 – Laboratory work in YNEGLH Central Lab

EGLN1	*EPO*	*HBA1*	*HBB*
EPAS1	*EPOR*	*HBA2*	*VHL*

R406.1 :: Thrombocythemia (Version 1.1)
https://panelapp.genomicsengland.co.uk/panels/945/
Agilent SureSelect Reagent Design ID: S3330962 – Laboratory work in YNEGLH Central Lab

JAK2	*MPL*	*SH2B3*	*THPO*

Gastrohepatology

R171: Cholestasis: SureSelect Gastrohepatology panel ID: Gastrohep v4 2022 Design ID: 3392981 (wet work in Leeds Central NEY GLH lab

ABCB11	*CYP7A1*	*LIPA*	*POLG*
ABCB4	*CYP7B1*	*MPI*	*RINT1*
ABCC2	*DCDC2*	*MPV17*	*SERPINA1*
ADK	*DGUOK*	*MVK*	*SLC25A13*
AKR1D1	*FAH*	*MYO5B*	*SMPD1*
ALDOB	*GALE*	*NBAS*	*TALDO1*
AMACR	*GALK1*	*NOTCH2*	*TJP2*
ATP7B	*GALT*	*NPC1*	*TRMU*
ATP8B1	*GBA1*	*NPC2*	*UGT1A1*
BAAT	*GBE1*	*NR1H4*	*UNC45A*
BCS1L	*HADHA*	*PEX1*	*USP53*
CFTR	*HNF1B*	*PEX12*	*VIPAS39*
CLDN1	*HSD3B7*	*PEX26*	*VPS33B*
COG7	*KIF12*	*PEX6*	*YARS1*
CYP27A1	*JAG1*	*PKHD1*	*ZFYVE19*

R173: Polycystic Liver disease (without polycystic kidney disease): SureSelect Gastrohepatology panel ID: Gastrohep v4 2022 Design ID: 3392981 (wet work in Leeds Central NEY GLH lab)

PRKCSH	*GANAB*	*PKD1*	*DNAJB11*
SEC63	*PKHD1*	*PKD2*	
LRP5	*ALG8*		

R193.a: Cystic renal disease and XR193.a (non-NHSE) SureSelect Gastrohepatology panel ID: Gastrohep v4 2022 Design ID: 3392981 (wet work in Leeds Central NEY GLH lab)

PKD1	*PKD2*

R193.b: Cystic renal disease and XR193.b (non-NHSE) SureSelect Gastrohepatology panel ID: Gastrohep v4 2022 Design ID: 3392981 (wet work in Leeds Central NEY GLH lab)

ALG8	*DZIP1L*	*LRP5*	*PKHD1*
ALG9	*GANAB*	*PKD1*	*REN*
DNAJB11	*HNF1B*	*PKD2*	*UMOD*

R331: Intestinal failure: SureSelect Gastrohepatology panel ID: Gastrohep v4 2022 Design ID: 3392981 (wet work in Leeds Central NEY GLH lab)

ADAM17	*EPCAM*	*NEUROG3*	*SLC9A3*
ADAMTS3	*FAT4*	*PCSK1*	*SPINT2*
ANGPTL3	*FBXL7*	*PLVAP*	*STX3*
AP1S1	*FLNA*	*RFX6*	*STXBP2*
APOB	*FOXP3*	*SAR1B*	*TERT*
ARX	*GUCY2C*	*SI*	*TMPRSS15*
CCBE1	*ICOS*	*SKIV2L*	*TREH*
CD55	*KMT2D*	*SLC10A2*	*TTC37*
CLMP	*LCT*	*SLC26A3*	*TTC7A*
CTLA4	*LRBA*	*SLC39A4*	*WNT2B*
DGAT1	*MTTP*	*SLC51B*	*XIAP*
EGFR	*MYO5B*	*SLC5A1*	

R172 Wilson Disease: S5 Gastrohepatology special panel ID: WG_IAD186831_improve.20191114 (wet work in Sheffield)

ATP7B			

R175: Pancreatitis: S5 Gastrohepatology special panel ID: WG_IAD186831_improve.20191114 (wet work in Sheffield)

PRSS1	*SPINK1*	*CFTR*	

R177: Hirschsprung disease: S5 Gastrohepatology special panel ID: WG_IAD186831_improve.20191114 (wet work in Sheffield)

RET			

Respiratory

(R189) Respiratory ciliopathies including non-CF bronchiectasis as PanelApp panel: Respiratory ciliopathies including non-CF bronchiectasis (Version 2.0) SureSelect Design ID: S3406032. Laboratory wetwork in NEYGLH Central lab

ARMC4	*CCDC65*	*DNAH11*	*HYDIN*	*PIK3R1*	*SCNN1B*
C11orf70	*CCNO*	*DNAH5*	*LRRC56*	*RAG1*	*SCNN1G*
C21orf59	*CFTR*	*DNAH9*	*LRRC6*	*RAG2*	*SPAG1*
CCDC103	*DNAAF1*	*DNAI1*	*MCIDAS*	*RSPH1*	*TTC25*
CCDC114	*DNAAF2*	*DNAI2*	*NFKB1*	*RSPH3*	*ZMYND10*
CCDC151	*DNAAF3*	*DNAL1*	*NFKB2*	*RSPH4A*	*GAS2L2*
CCDC39	*DNAAF4*	*DRC1*	*PIH1D3*	*RSPH9*	*OFD1*
CCDC40	*DNAAF5*	*GAS8*	*PIK3CD*	*SCNN1A*	*RPGR*

(R188) Pulmonary Arterial Hypertension as PanelApp panel: Pulmonary Arterial Hypertension (Version 3.0) SureSelect Design ID: S3406032. Laboratory wetwork in NEYGLH Central lab

ACVRL1	*KDR*
ATP13A3	*KCNK3*
BMPR2	*SMAD9*
EIF2AK4	*SOX17*
ENG	*TBX4*
GDF2	

(R186) Hereditary Haemorrhagic Telangiectasia as PanelApp panel: Hereditary Haemorrhagic Telangiectasia (Version 3.0) SureSelect Design ID: S3406032. Laboratory wetwork in NEYGLH Central lab

ACVRL1	*SMAD4*
ENG	*GDF2*
EPHB4	*RASA1*

(R139) Laterality disorders and isomerism as PanelApp panel: Laterality disorders and isomerism (Version 2.0) SureSelect Design ID: S3406032. Laboratory wetwork in NEYGLH Central lab

ARMC4	*CFAP53*	*DNAI1*	*SPAG1*
C11orf70	*DNAAF1*	*DNAI2*	*ZIC3*
C21orf59	*DNAAF3*	*GDF1*	*ZMYND10*
CCDC103	*DNAAF4*	*LRRC56*	*FOXJ1*
CCDC114	*DNAAF5*	*LRRC6*	*PKD1L1*
CCDC151	*DNAH11*	*MMP21*	
CCDC39	*DNAH5*	*NODAL*	
CCDC40	*DNAH9*	*PIH1D3*	

(R190) Pneumothorax as PanelApp panel: Pneumothorax - familial (Version 2.17) SureSelect Design ID: S3406032. Laboratory wetwork in NEYGLH Central lab

COL3A1	*TGFB3*
FBN1	*TGFBR1*
FLCN	*TGFBR2*
SERPINA1	*TSC1*
TGFB2	*TSC2*

(R192) Surfactant deficiency as PanelApp panel: Pneumothorax - familial (Version 1.2) SureSelect Design ID: S3406032. Laboratory wetwork in NEYGLH Central lab

ABCA3
NKX2-1
SFTPB
SFTPC

(R421) Pulmonary Fibrosis as PanelApp panel: Familial Pulmonary Fibrosis (Version 1.3) SureSelect Design ID: S3406032. Laboratory wetwork in NEYGLH Central lab

ACD	*MARS1*	*TERC*
AP3B1	*MUC5B*	*TERT*
CSF2RA	*NAF1*	*TINF2*
CSF2RB	*NHP2*	*ZCCHC8*
CTC1	*NOP10*	
DKC1	*PARN*	
HPS1	*RTEL1*	
HPS4	*SFTPA1*	

Oncology

Pharmacogenetics solid tumour panels:

Oncomine Focus NGS Assay (DNA and Fusions)	https://www.thermofisher.com/uk/en/home/clinical/preclinical-companion-diagnostic-development/oncomine-oncology/oncomine-focus-assay.html

Pan Cancer panels:

Illumina TruSight RNA fusion panel	https://www.illumina.com/content/dam/illumina-marketing/documents/products/gene_lists/gene_list_trusight_rna_fusion_panel.xlsx

Illumina TruSight Oncology 500 (TSO500)	https://www.illumina.com/content/dam/illumina/gcs/assembled-assets/marketing-literature/trusight-oncology-500-data-sheet-m-gl-00173/trusight-oncology-500-and-ht-data-sheet-m-gl-00173.pdf

Haemato Oncology panels:

Virtual Sub-Panel Gene Content (Myeloid panel):			
ANKRD26 (NM_014915.2)	***FBXW7*** (NM_033632.3)	***KRAS*** (NM_004985.4)	***SETBP1*** (NM_015559.2)
ASXL1 (NM_015338.5)	***FLT3*** (NM_004119.2)	***MPL*** (NM_005373.2)	***SF3B1*** (NM_012433.2)
BCOR (NM_001123385.1)	***GATA1*** (NM_002049.3)	***NF1*** (NM_001042492.2)	***SH2B3*** (NM_005475.2)
CALR (NM_004343.3)	***GATA2*** (NM_001145661.1)	***NFE2*** (NM_001261461.1)	***SRSF2*** (NM_003016.4)
CBL (NM_005188.2)	***GNB1*** (NM_002074.4)	***NOTCH1*** (NM_017617.4)	***STAG2*** (NM_001042749.2)
CEBPA (NM_004364.4)	***HRAS*** (NM_005343.2)	***NPM1*** (NM_002520.6)	***STAT3*** (NM_139276.2)
CSF3R (NM_156039.3)	***IDH1*** (NM_005896.3)	***NRAS*** (NM_002524.4)	***STAT5B*** (NM_012448.3)
CUX1 (NM_001913.4, NM_181552.3)	***IDH2*** (NM_002168.3)	***PHF6*** (NM_001015877.1)	***TET2*** (NM_001127208.2)
DDX41 (NM_016222.3)	***IKZF1*** (NM_006060.5)	***PPM1D*** (NM_003620.3)	***TP53*** (NM_000546.5)
DNMT3A (NM_175629.2)	***JAK2*** (NM_004972.3)	***PTEN*** (NM_000314.6)	***U2AF1*** (NM_006758.2)
ETNK1 (NM_018638.4)	***KIT*** (NM_000222.2)	***PTPN11*** (NM_002834.4)	***UBA1*** (NM_003334.3)
ETV6 (NM_001987.4)	***KMT2A*** (PTD)	***RAD21*** (NM_006265.2)	***WT1*** (NM_024426.4)

Technical information:

Library preparation: Twist Bioscience; **Sequencing**: Illumina NextSeq 550; **Analysis:** In-house pipeline, aligned to GRCh37p13, annotated using Alamut-batch. KMT2A-PTDs detected by exon coverage comparison (adapted from McKerrell et al., 2016) with SNP array confirmation for borderline cases.

Annotation Database: Catalogue of Somatic Mutations in Cancer (COSMIC) http://grch37-cancer.sanger.ac.uk/cosmic

Minimum Reporting Thresholds: 5% VAF (variant allele frequency) and 100X read depth at the identified genomic position. Note that thresholds for ARID1A and KMT2C are set at 20% VAF due to higher frequencies of technical artefacts for these genes.

This assay may not detect large-scale insertions/deletions (indels) >100bp. The lowest detectable VAF for large (>10bp) indels has not been determined. Low level KMT2A-PTDs (below ~20% VAF) may not be detected and the presence of an alternative copy number alteration affecting KMT2A cannot be fully excluded.

All variants are described using standard nomenclature according to the Human Genome Variation society (HGVS) guidelines (http://www.hgvs.org/). Numbering starts with c.1 at A of the ATG initiation codon.

The purpose of this test is to identify acquired variants that may be significant to the diagnosis, prognosis or treatment of haematological malignancy. **This test is not designed for minimal residual disease (MRD) monitoring**; the lower limit of detection is not adequate for this purpose and variants detected by this test would not necessarily represent suitable markers.

The results of this test should be interpreted in the context of the results of other testing and the clinical history of the patient. The results and interpretation given in this report are dependent upon correct sample labelling and accuracy of information provided on the referral form.

This test is optimised for the detection of acquired variants in cancer, but does not distinguish between acquired and inherited variants. The detection of inherited variants falls outside the intended use of this test. If there is a clinical suspicion of an inherited cancer syndrome, it is recommended that the clinician reviews the medical and family history of the patient, and if appropriate, should consider referral to their local Regional Clinical Genetics Service for germline testing.

Please note that this test is currently outside our UKAS Schedule of Accreditation.

Pan-HaemOnc Panel Full Gene List:

ABL1	*BTG2*	*CDKN2C*	*EP300*	*H2AC11*	*JAK3*	*MTOR*	*PDGFRB*	*RASA2*	*STK11*
AKT1	*BTK*	*CEBPA*	*ERBB2*	*H2AC17*	*KDM6A*	*MYB*	*PDS5B*	*RB1*	*SUZ12*
ALK	*CALR*	*CHEK2*	*ERBB3*	*H2AC6*	*KIT*	*MYC*	*PHF6*	*RHOA*	*SYK*
ANKRD26	*CARD11*	*CIITA*	*ETNK1*	*H2BC12*	*KLF2*	*MYD88*	*PIGA*	*ROS1*	*TBL1XR1*
ARAF	*CASP8*	*CKS1B*	*ETV6*	*H2BC4*	*KLHL6*	*NCOR2*	*PIK3CA*	*RPS15*	*TCF3*
ARID1A	*CBFB*	*CNOT3*	*EZH2*	*H2BC5*	*KMT2A*	*NF1*	*PIK3CB*	*RUNX1*	*TERT*
ARID1B	*CBL*	*CRBN*	*FAM46C*	*H2BC8*	*KMT2C*	*NF2*	*PIK3CD*	*SETBP1*	*TET2*
ARID2	*CCND1*	*CREBBP*	*FAS*	*H3C2*	*KMT2D*	*NFATC1*	*PIK3R1*	*SETD2*	*THRAP3*
ASXL1	*CCND2*	*CSF1R*	*FAT1*	*H3C8*	*KRAS*	*NFE2*	*PIM1*	*SETDB1*	*TLR2*
ASXL2	*CCND3*	*CSF3R*	*FAT3*	*HLA-A*	*LAMB4*	*NFKB1*	*PLCG2*	*SF1*	*TMEM30A*
ATM	*CCNE1*	*CTCF*	*FAT4*	*HRAS*	*LMO2*	*NFKB2*	*POT1*	*SF3B1*	*TNF*
ATRX	*CCR6*	*CTNNB1*	*FBXO11*	*ID3*	*LTB*	*NFKBIA*	*POU2AF1*	*SGK1*	*TNFAIP3*
B2M	*CD22*	*CUL4B*	*FBXW7*	*IDH1*	*LUC7L2*	*NFKBIE*	*POU2F2*	*SH2B3*	*TNFRSF14*
BCL10	*CD274*	*CUX1*	*FGFR1*	*IDH2*	*MAP2K1*	*NFKBIZ*	*PPM1D*	*SMARCA4*	*TP53*
BCL11A	*CD28*	*CXCR4*	*FGFR2*	*IKBKB*	*MAP2K4*	*NOTCH1*	*PRDM1*	*SMARCB1*	*TRAF2*
BCL2	*CD58*	*CYLD*	*FGFR3*	*IKZF1*	*MAP3K1*	*NOTCH2*	*PRKCB*	*SMC1A*	*TRAF3*
BCL6	*CD70*	*DDX3X*	*FLT3*	*IKZF3*	*MECOM*	*NPM1*	*PRPF8*	*SMC3*	*U2AF1*
BCL7A	*CD79A*	*DDX41*	*FOXO1*	*IL2RG*	*MED12*	*NRAS*	*PTCH1*	*SOCS1*	*U2AF2*
BCOR	*CD79B*	*DIS3*	*GATA1*	*IL7R*	*MEF2B*	*NSD2*	*PTEN*	*SPEN*	*UBA1*
BCORL1	*CD83*	*DNMT3A*	*GATA2*	*IRF1*	*MET*	*NTRK1*	*PTPN11*	*SPIB*	*UBR5*
BIRC2	*CDK4*	*DTX1*	*GATA3*	*IRF4*	*MGA*	*P2RY8*	*PTPN6*	*SRSF2*	*VAV1*
BIRC3	*CDK6*	*EBF1*	*GNA13*	*IRF8*	*MPEG1*	*PAX5*	*PTPRC*	*STAG2*	*WT1*
BLM	*CDKN1B*	*EGFR*	*GNAS*	*ITPKB*	*MPL*	*PDCD1*	*PTPRD*	*STAT3*	*XPO1*
BRAF	*CDKN2A*	*EGR1*	*GNB1*	*JAK1*	*MSH2*	*PDCD1LG2*	*RAD21*	*STAT5B*	*ZFP36L1*
BTG1	*CDKN2B*	*EGR2*	*GPRC5A*	*JAK2*	*MSH6*	*PDGFRA*	*RAD51*	*STAT6*	*ZRSR2*