Targeted sequencing with the Ion Torrent System is able to identify single nucleotide variants, small insertions and small deletions. Variants in repeat sequences, large homopolymers and large insertions/deletions are not or difficult to identify.

The designed BMF Panel (IAD156379_243) consists of 3140 amplicons and is covering 861,9 Kbase. 99,1% of desired areas (exons, flanking intronic regions, untranslated regions and promotor areas) are covered from the following 180 genes:

Overview genes present in BMF-panel									
ABCA1	BLOC1S3	CXCR4	FANCE	HPS1	MAP2K2	PMS2	RPL35A	SAMD9L	THPO
ABCB7	BLOC1S6	CYCS	FANCF	HPS3	MASTL	PRF1	RPL36	SBDS	TINF2
ABCG5	BRCA1	DDX41	FANCG	HPS4	MKL1	PTPN11	RPL5	SBF2	TP53
ABCG8	BRCA2	DHFR	FANCI	HPS5	MLPH	RAB27A	RPS10	SEC23B	TPM4
ACBD5	BRIP1	DKC1	FANCL	HPS6	MPL	RAC2	RPS14	SH2D1A	TPP1
ACD	C15orf41	DNAJC21	FANCM	IKZF1	MTHFD1	RAD51	RPS15	SLC37A4	UBE2T
ACTB	C6orf25	DTNBP1	FAS	IL2RG	MYO5A	RAD51C	RPS15A	SLFN14	UNC13D
ADA	CBL	ELANE	FASLG	ITK	NBEAL2	RBM8A	RPS17	SLX4	USB1
ADA2	CDAN1	EPCAM	FLI1	JAGN1	NBN	RIT1	RPS19	SMARCD2	VIPAS39
AK2	CDC42	ERCC4	FYB	JAK2	NF1	RMRP	RPS24	SOS1	VPS33B
ALAS2	CEBPA	ERCC6L2	G6PC3	KLF1	NOLA2	RNF168	RPS26	SRC	VPS45
ANKRD26	CEBPE	ETV6	GATA1	KRAS	NOLA3	RPL10	RPS27	SRP72	WAS
AP3B1	CLPB	EVI1	GATA2	LAMTOR2	NRAS	RPL11	RPS28	STX11	WDR1
AP3D1	COX4-1	FADD	GFI1	LIG4	PALB2	RPL15	RPS29	STXBP2	WIPF1
ASXL1	CSF2RA	FANCA	GFI1B	LYST	PARN	RPL26	RPS7	TAZ	WRAP53
ATM	CSF3R	FANCB	GINS1	MAD2L2	PGM3	RPL27	RTEL1	TCIRG1	XIAP
ATRX	CTC1	FANCC	HAX1	MAGT1	PLAU	RPL27A	RUNX1	TERC	XRCC2
BLM	CTSC	FANCD2	HOXA11	MAP2K1	PLCB2	RPL31	SAMD9	TERT	YARS2

Genes present in BMF-panel

The percentage of target bases that is covered at least 20 times (%Base20x) is at least 99,0% for the recommended Mapped Reads of 4.000.000. For 69 different genes a few bases are missed, either in the design or due to practical coverage, as listed in Part 1 of the table below. Some pathogenic variants listed in the HGMD database are missed as well, as can be seen in part 2 of this table.

Part 1: Missed in newly designed regions

Gene	chromosome	coordinate start	coordinate end	Exon	% Gene covered	Missed number of bases	HGMD 2	HGMD Accession
UBE2T	chr1	202302132	202302150	6	97.3	18	No	
ABCG8	chr2	44099190	44099204	7	99.4	14	No	
WIPF1	chr2	175436959	175436965	5	99.6	6	No	
RPL15	chr3	23963097	23963171	5	89.9	74	No	
NBEAL2	chr3	47047054	47047065	41	99.8	11	No	
NBEAL2	chr3	47037061	47037071	13		10	No	
TERC	chr3	169482689	169482699	1	98.6	10	Yes	CR116665
FANCD2	chr3	10103886	10103893	20	99.9	7	No	
DDX41	chr5	176939525	176939537	14	99.4	12	No	
TERT-promotor-3	chr5	1297749	1297751	Promotor	99.7	2	No	
STX11	chr6	144508199	144508220	2	97.6	21	No	
PMS2	chr7	6026384	6026417	11	98.3	33	Yes	CS152766, CM1612933, CM102798
PMS2-promotor	chr7	6046788	6046805	Promotor		17	No	
CYCS	chr7	25163347	25163369	3	93.5	22	No	
IKZF1	chr7	50468146	50468153	8	99.7	7	No	
HOXA11	chr7	27224335	27224339	1	99.6	4	No	
MASTL	chr10	27470403	27470427	11	99.1	24	No	
PRF1	chr10	72358206	72358221	3	98.2	15	Yes	CM150717, CM071931
PRF1	chr10	72360464	72360479	2		15	Yes	CD060649, CM992949
ACBD5	chr10	27499737	27499749	8	99.3	12	No	
HPS6	chr10	103827164	103827176	1	99.5	12	No	
HPS1	chr10	100189393	100189404	10	99.5	11	No	
CTSC-promotor	chr11	88070871	88070883	Promotor	94.0	12	No	
HPS5	chr11	18332994	18333003	4	99.8	9	No	
YARS2	chr12	32908535	32908548	1	99.1	13	No	
BRCA2	chr13	32930559	32930591	15	99.7	32	Yes	CD105867, CS107521, CS1213349, CM175565, CM127115, CM1313772
FANCM	chr14	45646163	45646176	14	99.8	13	No	
CEBPE	chr14	23588130	23588134	1	99.5	4	No	
C15orf41	chr15	37039243	37039256	11	98.8	13	No	
BLOC1S6	chr15	45897709	45897717	4	98.8	8	No	
CDAN1	chr15	43028564	43028570	2	99.9	6	No	
RAD51	chr15	40994053	40994055	4	99.8	2	No	
FANCA	chr16	89882939	89883026	1	98.1	87	Yes	13 mutations
FANCA-splice-6	chr16	89818848	89818864	letween 30-31		16	No	
ACD	chr16	67691541	67691555	12	99.2	14	No	
SLX4	chr16	3640387	3640395	12	99.7	8	No	
SLX4	chr16	3639010	3639013	12		3	No	
SLX4	chr16	3633449	3633456	14		7	No	
UNC13D	chr17	73838954	73838992	5	97.4	38	Yes	CM137109
UNC13D	chr17	73832484	73832487	15		3	No	
UNC13D	chr17	73831861	73831863	19		2	No	
UNC13D	chr17	73830588	73830617	23		29	No	
UNC13D	chr17	73831484	73831505	20		21	Yes	CS141343, CM113892, CS066316, CD033243
BRCA1-splice-15	chr17	41199767	41199783	letween 22-2	99.3	16	No	
BRCA1-promotor	chr17	41279315	41279331	Promotor		16	No	
BRCA1-promotor	chr17	41197112	41197127	Promotor		15	No	
SMARCD2	chr17	61919814	61919815	1	99.9	1	No	
AP3D1	chr19	2121076	2121091	14	99.5	15	No	
AP3D1	chr19	2129083	2129087	8		4	Yes	
TPM4	chr19	16212068	16212074	8	97.2	6	No	
TPM4	chr19	16187393	16187410	1		17	No	
TPM4	chr19	16186919	16186927	2		8	No	
CEBPA-promotor	chr19	33754523	33754539	Promotor	91.6	16	No	
CEBPA	chr19	33792683	33792701	1		18	No	
CEBPA	chr19	33792835	33792848	1		13	No	
KLF1	chr19	12996653	12996665	2	98.9	12	No	
STXBP2	chr19	7703899	7703911	3	99.1	12	Yes	CS108415
STXBP2	chr19	7712395	7712402	18		7	Yes	CS125307
ASXL1	chr20	30946599	30946640	1	99.1	41	No	
SEC23B-splice-4	chr20	18508006	18508029	Between 8-9	88.5	23	No	
RTEL1	chr20	62321748	62321766	26	99.2	18	No	
RTEL1	chr20	62326840	62326855	34		15	No	
HPS4	chr22	26860173	26860187	11	99.3	14	No	
HPS4	chr22	26859877	26859879	11		2	No	
MKL1	chr22	40814697	40814718	12	98.7	21	No	
MKL1	chr22	40807585	40807596	15		11	No	
MKL1	chr22	40815297	40815302	12		5	No	
CSF2RA	chrX	1422148	1422260	9	93.2	112	No	
RPL10	chrX	153628963	153628972	6	99.0	9	No	
DKC1	chrX	154001526	154001529	11	99.8	3	No	
					Total bases miss	1147		

Part 2: Missed by coverage in experiments in almost all samples

Gene	chromosome	coordinate start	coordinate end	Exon	% Gene covered	Missed nr of bases of Submitted	HGMD 2018.2	HGMD Accession
ANKRD26	chr10	27349462	27349620	14	99.7	13	No	
HPS1	chr10	100183872	100184199	14	97.1	67	Yes	CM1618690, CM163884 & CP025155
SBF2	chr11	9810885	9810983	35	99.8	10	No	
TCIRG1	chr11	67811305	67811357	8/9	99.4	18	Yes	CD1210328
ATM	chr11	108163190	108163353	30	99.8	13	Yes	CS031767
CBL	chr11	119077212	119077385	1	96.0	116	No	
LIG4-promotor	chr13	108867388	108867629	Promotor	91.5	241	No	
MYO5A	chr15	52611511	52611588	38	99.4	34	No	
MAP2K1	chr15	66735601	66735905	4	93.2	88	Yes	CM1513642
NF1-promotor	chr17	29421955	29422226	Promotor	97.1	271	Yes	4 mutations
UNC13D	chr17	73827305	73827634	26	96.9	116	Yes	8 mutations
AP3D1	chr19	2118826	2118881	15	99.7	11	No	
MAP2K2	chr19	4123509	4124085	1	92.6	97	No	
STXBP2	chr19	7710985	7711305	16	95.0	106	Yes	CM096296 & CS1716304
BLOC1S3	chr19	45682811	45682877	2	89.2	67	No	
ASXL1	chr20	30946297	30946599	1	99.6	21	No	
SRC	chr20	36012768	36013065	4	97.4	44	No	
DNAJC21	chr5	34929759	34929939	1	99.2	15	Yes	CM183345
FYB	chr5	39127673	39127991	11	97.5	67	No	
RMRP	chr9	35657618	35657876	1	53.6	129	Yes	38 mutations
ERCC6L2	chr9	98690162	98690479	10	98.3	82	No	
CSF2RA	chrX	1412940	1413227	6	99.3	12	Yes	CM109619
			Total bases missed:			1638		

Some additional regions might be missed in a sample, due to low coverage or uniformity.

Part 3: Missed by coverage in experiments in a few samples

Gene	chromosome	coordinate start	coordinate end	Exon	% Gene covered	Missed nr of bases of Submitted	HGMD 2018.2	HGMD Accession
HPS1	chr10	100185094	100185336	13	98.1	43	Yes	CI962293
CLPB	chr11	72069826	72070150	6	94.2	139	Yes	4 mutations
SMARCD2	chr17	61919817	61919852	1	97.9	36	No	
UNC13D	chr17	73828955	73829058	25	99.5	17	No	CX113889 & CI1712765
ABCG5	chr2	44051958	44052279	7	93.3	140	Yes	CM104323 & CI092640
HPS4	chr22	26868654	26868886	5	95.9	94	No	
MKL1	chr22	40819484	40819782	9	94.7	160	No	
WDR1	chr4	10117984	10118280	1	99.4	11	No	
WAS	chrX	48547120	48547249	5	92.0	130	Yes	31 mutations
FANCM	chr14	45652913	45653015	17	99.3	44	No	
CDAN1	chr15	43028571	43028699	2	96.7	129	Yes	4 mutations
BRCA1-promotor	chr17	41196263	41196516	24	96.3	254	Yes	CD123597 & CR123596
DHFR	chr5	79950299	79950620	1	98.6	10	No	

Reporting

Only clinical relevant variants will be reported. Variants with classification *Certainly Pathogenic* (class 5) and *Likely Pathogenic* (class 4) are always reported. Variants with category *Unknown significance* (class 3) will only be reported if the variant is expected to be involved in the phenotype of the patient. Category *Certainly Benign* (class 1) and *Likely Benign* (class 2) variants will not be reported. (see: *Document: Practice Guidelines for the Evaluation of Pathogenicity and the Reporting of Sequence Variants in Clinical Molecular Genetics*)

Besides reporting the clinical relevant variants we report whether a patient is heterozygous, homozygous, expected compound heterozygous or hemizygous for a mutation and how this may relate to disease phenotype.

All the variants are annotated and reported as designated by the Human Genome Variation Society (HGVS) nomenclature, as described at their website http://varnomen.hgvs.org