Blueprint Genetics

Sample report as of June 14th, 2022. Regional differences may apply. For complete and up-to-date test methodology description, please see your report in Nucleus online portal. Accreditation and certification information available at ***blueprintgenetics.com/certifications***

Hereditary Leukemia Panel (Hereditary Cancer) Plus

REFERRING HEALTHCARE PROFESSIONAL

NAME	HOSPITAL

PATIENT

NAME	DOB	AGE	GENDER	ORDER ID
		53		

PRIMARY SAMPLE TYPE	SAMPLE COLLECTION DATE	CUSTOMER SAMPLE ID
Blood		

SUMMARY OF RESULTS

PRIMARY FINDINGS

DNA sample is isolated from blood and patient has hematological disorder, and therefore the identified variants may represent either germline or somatic mutations. We recommend using DNA samples extracted from skin cells in order to study only germline mutations in this patient.

TP53 c.577C>T, p.(His193Tyr) was identified in this patient. The variant is likely pathogenic. The test result suggests that the patient is mosaic for the detected variant.

Del/Dup (CNV) analysis

Negative for explaining the patient's phenotype.

PRIMARY FINDINGS: SEQUENCE ALTERATIONS

GENE	TRANSCRIPT	NOMENCLATURE	GENOTYPE	CONSEQUENCE	INHERITANCE	CLASSIFICATION
TP53	NM_000546.5	c.577C>T, p.(His193Tyr)	HET	missense_variant	AD	**Likely pathogenic**

ID	ASSEMBLY	POS	REF/ALT
	GRCh37/hg19	17:7578272	G/A

gnomAD AC/AN	POLYPHEN	SIFT	MUTTASTER	PHENOTYPE
0/0	probably damaging	deleterious	disease causing	Adrenocortical carcinoma, Breast cancer, familial, Choroid plexus papilloma, Colorectal cancer, Ependymoma, intracranial, Hepatoblastoma, Li-Fraumeni syndrome, Non-Hodgkin lymphoma, Osteogenic sarcoma

SEQUENCING PERFORMANCE METRICS

PANEL	GENES	EXONS / REGIONS	BASES	BASES > 20X	MEDIAN COVERAGE	PERCENT > 20X
Hereditary Leukemia Panel (Hereditary Cancer)	42	696	143422	143422	172	100

TARGET REGION AND GENE LIST

The Blueprint Genetics Hereditary Leukemia Panel Plus Analysis includes sequence analysis and copy number variation analysis of the following genes: *ANKRD26, ATM, BLM, BRAF*, BRCA1*, BRCA2, CBL, CDKN2A, CEBPA, DDX41, DKC1, EFL1*, EPCAM, ETV6, FANCA, GATA2, HAVCR2, HRAS, IKZF1, KRAS*, MAP2K1, MAP2K2, MLH1, MSH2, MSH6, NBN, NF1*, NRAS, PAX5, PMS2*, PTPN11, RIT1, RUNX1, SAMD9, SAMD9L, SBDS*, SOS1, SRP72*, TERC, TERT, TINF2 and TP53.* This panel targets protein coding exons, exon-intron boundaries (± 20 bps) and selected noncoding, deep intronic variants (listed in Appendix 5). This panel should be used to detect single nucleotide variants and small insertions and deletions (INDELs) and copy number variations defined as single exon or larger deletions and duplications. This panel should not be used for the detection of repeat expansion disorders or diseases caused by mitochondrial DNA (mtDNA) mutations. The test does not recognize balanced translocations or complex inversions, and it may not detect low level mosaicism.

*Some, or all, of the gene is duplicated in the genome. Read more: https://blueprintgenetics.com/pseudogene/
The sensitivity to detect variants may be limited in genes marked with an asterisk (*).

STATEMENT

CLINICAL HISTORY

This tested sample is the DNA isolated from the blood of a 53-year-old individual with MDS-EB1, with worsening cytopenias and 7% blasts. There is a family history of acute myeloid leukemia.

CLINICAL REPORT

Sequence analysis using the Blueprint Genetics (BpG) Hereditary Leukemia Panel identified a missense variant *TP53* c.577C>T, p.(His193Tyr). The *TP53* c.577C>T, p.(His193Tyr) variant was detected in the NGS run in 14% (36 out of 249) of the reads.

TP53 c.577C>T, p.(His193Tyr)

This variant is absent in the Genome Aggregation Database control population cohorts (gnomAD, n>120,000 exomes and >15,000 genomes). All *in silico* tools utilized predict this variant to be damaging to protein structure and function. The *TP53* c.577C>T, p.(His193Tyr) variant has been detected by other laboratories in the context of clinical testing and submitted to ClinVar (variation ID 230256). In ClinVar it has been reported as a germline variant in three individuals of which one was reported as affected (condition not shown). It has also been detected as a somatic variant in several individuals in association with different cancer types including stomach and intestine cancer, hepatocellular carcinoma, neoplasms of the breast and the brain, squamous cell lung carcinoma, pancreatic adenocarcinoma, gynecological cancers, chronic lymphocytic leukemia (CLL), and acute myeloid leukemia (AML) (ClinVar variation ID 230256). The p.(His193Tyr) change has been shown to result in nonfunctional p53 (PMID: 21514416). The *TP53* c.577C>T, p.(His193Tyr) variant has also been reported with VAF 98% in a patient with glioma in a systematic analysis of *TP53* somatic mutation data extracted from the IARC TP53 Database and from genomic data repositories (PMID: 27328919). In addition, other missense variants affecting the same codon, p.(His193Arg), p.(His193Asp), p.(His193Leu), and p.(His193Pro) have been reported as germline variants in patients with Li-Fraumeni syndrome (including PMID: 7887414, 25945745, 28369373, 28152038, 18685109) and as a somatic variant in several cancer types (ClinVar ID 376613, 376614), supporting the functional importance of histidine at position 193.

TP53

The *TP53* (MIM *191170) gene encodes a tumor suppressor protein p53 that contains transcriptional activation, DNA binding, and oligomerization domains. It responds to diverse cellular stresses to regulate expression of target genes, thereby inducing cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism (PMID: 17380161). Although p53 has been shown to be involved in diverse regulatory pathways, its best characterized role is in protecting against cancer development. The loss of p53 function decreases the likelihood that cells with genetic errors will be flagged for DNA repair or apoptosis, enabling these cells to further proliferate resulting in a colony of abnormal cells and eventually a malignant tumor. Mutations in *TP53* have been associated with an increased susceptibility to a variety of cancers, including hereditary cancers such as Li-Fraumeni syndrome (LFS; MIM #151623). LFS is a cancer predisposition syndrome characterized by an autosomal dominant inheritance and early onset of tumors, multiple tumors within an individual, and multiple affected family members (GeneReviews NBK1311). The most common types of tumors are soft tissue sarcoma, osteosarcoma, premenopausal breast cancer, brain tumors, leukemia, and adrenocortical carcinoma. In addition, renal cell carcinomas, as well as endometrial, ovarian, prostate and gonadal germ cell tumors have been reported in families with LFS (GeneReviews NBK1311). *TP53* variants may also affect response to anticancer and also other treatments and medication (PMID 25981898, 17613549). The penetrance of LFS is high: the lifetime risk for cancer is estimated to be nearly 100% for females and about 70% for males by the age of 70 years (PMID: 10864200; 16912210). Around 80% of families with LFS have an identifiable *TP53* pathogenic variant (PMID: 21779515), while it has been estimated that the prevalence of these mutations ranges from 1/10,000 to 1/25,000 (ORPHA524). Most *TP53* pathogenic variants are located within exons 5-8, which encode the core DNA-binding region of the gene.

Currently, there is evidence of early tumor detection through surveillance to be associated with improved long-term survival in children and adults with germline *TP53* pathogenic variants (PMID: 27501770). Currently, it is recommended that: (1) children and adults undergo comprehensive regular physical examination; (2) children and adults be encouraged to see a physician promptly for evaluation of lingering symptoms and illnesses; (3) women undergo breast cancer monitoring, with annual breast MRI and twice annual clinical breast examination beginning at age 20-25 years (GeneReviews NBK1311). The use of mammograms has been controversial because of radiation exposure and limited sensitivity. When included, annual mammograms should alternate with breast MRI, with one modality every six months; (4) adults consider routine screening for colorectal cancer with colonoscopy every 2-3 years beginning no later than age 25 years; (5) individuals consider organ-targeted surveillance based on the pattern of cancer observed in their family. Intensified surveillance with whole-body MRI protocols for adults and children who carry a germline *TP53* pathogenic variant are being evaluated in investigational settings.

A pathogenic heterozygous *TP53* variant may be inherited in an autosomal dominant manner (cancer predisposition syndrome known as Li-Fraumeni syndrome) and the second variant or loss of heterozygosity (LOH) may occur as somatic mutation in smaller cell population and act as a "driver mutation" during the tumorigenesis (PMID: 9047394).

Somatic mutations in the *TP53* gene are one of the most frequent alterations in human cancers.

Loss-of-function is a disease-causing mechanism for the *TP53* gene and currently HGMD Professional 2020.1 lists more than 500 disease-causing variants. These include 7% nonsense, 51% missense, 9% splicing, 19% small deletions, 5% insertions, 2% small indels, 6% gross deletions, 0.4% gross insertions and 0.6% complex rearrangements.

Mutation nomenclature is based on GenBank accession NM_000546.5 (*TP53*) with nucleotide one being the first nucleotide of the translation initiation codon ATG.

CONCLUSION

TP53 c.577C>T, p.(His193Tyr) is classified as likely pathogenic, based on the variant's absence in control populations, *in silico* predicted pathogenicity, identification of the variant as somatic in several individuals with cancer, and functional assay data. Genetic counseling and family member testing are recommended. The variant observed in this patient is present only in 14% of the NGS-reads (observed 14% T and 86% C) whereas a 50:50 allele distribution would be expected in cases of germline heterozygosity. These results suggest that the variant might be somatic.

Since DNA sample is isolated from blood, we recommend using DNA sample extracted from skin cells in order to study only germline variants in this patient.

STEP	DATE
Order date	
Sample received	
Sample in analysis	
Reported	

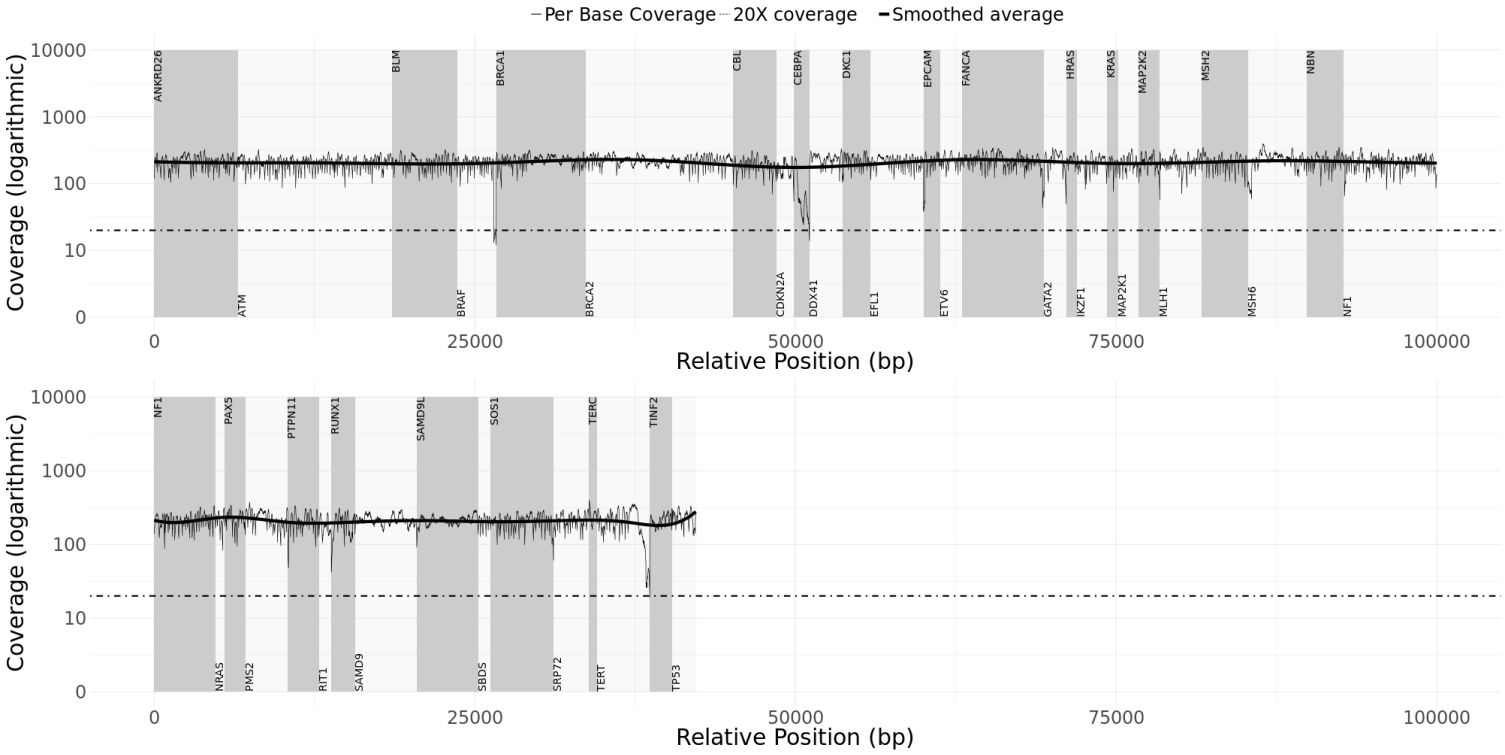
(This statement has been prepared by our geneticists and physicians, who have together evaluated the sequencing results.)

Signature

Name

Title

Readability of the coverage plot may be hindered by faxing. A high quality coverage plot can be found with the full report on nucleus.blueprintgenetics.com.



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APPENDIX 5: SUMMARY OF THE TEST

PLUS ANALYSIS

Laboratory process: When required, the total genomic DNA was extracted from the biological sample using bead-based method. DNA quality and quantity were assessed using electrophoretic methods. After assessment of DNA quality, qualified genomic DNA sample was randomly fragmented using non-contact, isothermal sonochemistry processing. Sequencing library was prepared by ligating sequencing adapters to both ends of DNA fragments. Sequencing libraries were size-selected with bead-based method to ensure optimal template size and amplified by polymerase chain reaction (PCR). Regions of interest (exons and intronic targets) were targeted using hybridization-based target capture method. The quality of the completed sequencing library was controlled by ensuring the correct template size and quantity and to eliminate the presence of leftover primers and adapter-adapter dimers. Ready sequencing libraries that passed the quality control were sequenced using the Illumina's sequencing-by-synthesis method using paired-end sequencing (150 by 150 bases). Primary data analysis converting images into base calls and associated quality scores was carried out by the sequencing instrument using Illumina's proprietary software, generating CBCL files as the final output.
Bioinformatics and quality control: Base called raw sequencing data were transformed into FASTQ format using Illumina's software (bcl2fastq). Sequence reads of each sample were mapped to the human reference genome (GRCh37/hg19). Burrows-Wheeler Aligner (BWA-MEM) software was used for read alignment. Duplicate read marking, local realignment around indels, base quality score recalibration and variant calling were performed using GATK algorithms (Sentieon) for nDNA. Variant data for were annotated using a collection of tools (VcfAnno and VEP) with a variety of public variant databases including but not limited to gnomAD, ClinVar and HGMD. The median sequencing depth and coverage across the target regions for the tested sample were calculated based on MQ0 aligned reads. The sequencing run included in-process reference sample(s) for quality control, which passed our thresholds for sensitivity and specificity. The patient's sample was subjected to thorough quality control measures including assessments for contamination and sample mix-up. Copy number variations (CNVs), defined as single exon or larger deletions or duplications (Del/Dups), were detected from the sequence analysis data using a proprietary bioinformatics pipeline. The difference between observed and expected sequencing depth at the targeted genomic regions was calculated and regions were divided into segments with variable DNA copy number. The expected sequencing depth was obtained by using other samples processed in the same sequence analysis as a guiding reference. The sequence data were adjusted to account for the effects of varying guanine and cytosine content.
Interpretation: The clinical interpretation team assessed the pathogenicity of the identified variants by evaluating the information in the patient requisition, reviewing the relevant scientific literature and manually inspecting the sequencing data if needed. All available evidence of the identified variants was compared to classification criteria. Reporting was carried out using HGNC-approved gene nomenclature and mutation nomenclature following the HGVS guidelines. Likely benign and benign variants were not reported.
Variant classification: Our variant classification follows the Blueprint Genetics Blueprint Genetics Variant Classification Schemes modified from the ACMG guideline 2015. Minor modifications were made to increase reproducibility of the variant classification and improve the clinical validity of the report.
Databases: The pathogenicity potential of the identified variants were assessed by considering the predicted consequence of the change, the degree of evolutionary conservation as well as the number of reference population databases and mutation databases such as, but not limited to, the gnomAD, ClinVar, HGMD Professional and Alamut Visual. In addition, the clinical relevance of any identified CNVs was evaluated by reviewing the relevant literature and databases such as Database of Genomic Variants and DECIPHER. For interpretation of mtDNA variants specific databases including e.g. Mitomap, HmtVar and 1000G were used.
Confirmation of sequence alterations: Sequence variants classified as pathogenic, likely pathogenic and variants of uncertain significance (VUS) were confirmed using bi-directional Sanger sequencing when they did not meet our stringent NGS quality metrics for a true positive call. In addition, prenatal case with diagnostic findings were confirmed.
Confirmation of copy number variants: CNVs (Deletions/Duplications) were confirmed using a digital PCR assay if they covered less than 10 exons (heterozygous), less than 3 exons (homo/hemizygous) or were not confirmed at least three times previously at our laboratory. Furthermore, CNVs of any size were not confirmed when the breakpoints of the call could be

determined.

Analytic validation: The detection performance of this panel is expected to be in the same range as our high-quality, clinical grade NGS sequencing assay used to generate the panel data (nuclear DNA: sensitivity for SNVs 99.89%, indels 1-50 bps 99.2%, one-exon deletion 100% and five exons CNV 98.7%, and specificity >99.9% for most variant types). It does not detect very low level mosaicism as a variant with minor allele fraction of 14.6% can be detected in 90% of the cases. Detection performance for mtDNA variants (analytic and clinical validation): sensitivity for SNVs and INDELs 100.0% (10-100% heteroplasmy level), 94.7% (5-10% heteroplasmy level), 87.3% (<5% heteroplasmy level) and for gross deletions 100.0%. Specificity is >99.9% for all.

Test restrictions: A normal result does not rule out the diagnosis of a genetic disorder since some DNA abnormalities may be undetectable by the applied technology. Test results should always be interpreted in the context of clinical findings, family history, and other relevant data. Inaccurate or incomplete information may lead to misinterpretation of the results.

Technical limitations: This test does not detect the following: complex inversions, gene conversions, balanced translocations, repeat expansion disorders unless specifically mentioned, noncoding variants deeper than ±20 base pairs from exon-intron boundary unless otherwise indicated (please see the list of noncoding variants covered by the test). Additionally, this test may not reliably detect the following: low level mosaicism, stretches of mononucleotide repeats, indels larger than 50bp, single exon deletions or duplications, and variants within pseudogene regions/duplicated segments. The sensitivity of this test may be reduced if DNA is extracted by a laboratory other than Blueprint Genetics. Laboratory error is also possible. Please see the Analytic validation above.

Regulation and accreditations: This test was developed and its performance characteristics determined by Blueprint Genetics (see Analytic validation). It has not been cleared or approved by the US Food and Drug Administration. This analysis has been performed in a CLIA-certified laboratory (#99D2092375), accredited by the College of American Pathologists (CAP #9257331) and by FINAS Finnish Accreditation Service, (laboratory no. T292), accreditation requirement SFS-EN ISO 15189:2013. All the tests are under the scope of the ISO 15189 accreditation (excluding mtDNA testing and digital PCR confirmation).

NONCODING VARIANTS COVERED BY THE PANEL:

NM_014915.2(ANKRD26):c.-116C>G
NM_014915.2(ANKRD26):c.-118C>A
NM_014915.2(ANKRD26):c.-119C>A
NM_014915.2(ANKRD26):c.-119C>A/G
NM_014915.2(ANKRD26):c.-121A>C
NM_014915.2(ANKRD26):c.-127_-126delAT
NM_014915.2(ANKRD26):c.-126T>C
NM_014915.2(ANKRD26):c.-126T>G
NM_014915.2(ANKRD26):c.-127A>G
NM_014915.2(ANKRD26):c.-127A>T
NM_014915.2(ANKRD26):c.-128G>T
NM_014915.2(ANKRD26):c.-128G>A
NM_014915.2(ANKRD26):c.-128G>C
NM_014915.2(ANKRD26):c.-134G>A
NM_000051.3(ATM):c.-174A>G
NM_000051.3(ATM):c.-31+595G>A
NM_000051.3(ATM):c.-30-1G>T
NM_000051.3(ATM):c.2639-384A>G
NM_000051.3(ATM):c.2839-579_2839-576delAAGT
NM_000051.3(ATM):c.3403-12T>A
NM_000051.3(ATM):c.3994-159A>G
NM_000051.3(ATM):c.4612-12A>G
NM_000051.3(ATM):c.5763-1050A>G
NM_000051.3(ATM):c.8418+681A>G
NM_007294.3(BRCA1):c.*1340_*1342delTGT
NM_007294.3(BRCA1):c.*1271T>C

NM_007294.3(BRCA1):c.*528G>C
NM_007294.3(BRCA1):c.*103_*106delTGTC
NM_007294.3(BRCA1):c.*58C>T
NM_007294.3(BRCA1):c.5468-40T>A
NM_007294.3(BRCA1):c.5407-25T>A
NM_007294.3(BRCA1):c.5333-36_5333-22delTACTGCAGTGATTTT
NM_007294.3(BRCA1):c.5277+2916_5277+2946delAAATTCTAGTGCTTTGGATTTTTTCCTCCATinsGG
NM_007294.3(BRCA1):c.5194-12G>A
NM_007294.3(BRCA1):c.5075-27delA
NM_007294.3(BRCA1):c.442-22_442-13delTGTTCTTTAC
NM_007294.3(BRCA1):c.213-11T>G
NM_007294.3(BRCA1):c.213-12A>G
NM_007294.3(BRCA1):c.213-15A>G
NM_007294.3(BRCA1):c.-19-2A>G
NM_000059.3(BRCA2):c.-40+1G>A
NM_000059.3(BRCA2):c.-39-89delC
NM_000059.3(BRCA2):c.-39-1_-39delGA
NM_000059.3(BRCA2):c.-39-1G>A
NM_000059.3(BRCA2):c.426-12_426-8delGTTTT
NM_000059.3(BRCA2):c.8488-14A>G
NM_000059.3(BRCA2):c.8954-15T>G
NM_000059.3(BRCA2):c.9502-28A>G
NM_000059.3(BRCA2):c.9502-12T>G
NM_000077.4(CDKN2A):c.458-105A>G
NM_000077.4(CDKN2A):c.151-1104C>G
NM_000077.4(CDKN2A):c.150+1104C>A
NM_058197.4(CDKN2A):c.*73+2T>G
NM_000077.4(CDKN2A):c.-21C>T
NM_000077.4(CDKN2A):c.-49C>A
NM_000077.4(CDKN2A):c.-56G>T
NM_000077.4(CDKN2A):c.-93_-91delAGG
NM_001363.3(DKC1):c.-142C>G
NM_001363.3(DKC1):c.-141C>G
NM_001363.3(DKC1):c.85-15T>C
NM_002354.2(EPCAM):c.556-14A>G
NM_000135.3(FANCA):c.4261-19_4261-12delACCTGCTC
NM_000135.2(FANCA):c.3239+82T>G
NM_000135.2(FANCA):c.2982-192A>G
NM_000135.2(FANCA):c.2778+83C>G
NM_000135.2(FANCA):c.2504+134A>G
NM_000135.2(FANCA):c.2223-138A>G
NM_000135.2(FANCA):c.1567-20A>G
NM_000135.2(FANCA):c.893+920C>A
NM_032638.4(GATA2):c.1017+572C>T
NM_032638.4(GATA2):c.1017+513_1017+540delGGAGTTTCCTATCCGGACATCTGCAGCC
NM_032638.4(GATA2):c.1017+532T>A
NM_000249.3(MLH1):c.-413_-411delGAG
NM_000249.3(MLH1):c.-107C>G
NM_000249.3(MLH1):c.-63_-58delGTGATTinsCACGAGGCACGAGCACGA
NM_000249.3(MLH1):c.-42C>T
NM_000249.3(MLH1):c.-27C>A

NM_000249.3(MLH1):c.116+106G>A
NM_000249.3(MLH1):c.117-11T>A
NM_000249.3(MLH1):c.454-13A>G
NM_000249.3(MLH1):c.885-9_887dupTCCTGACAGTTT
NM_000249.3(MLH1):c.1558+13T>A
NM_000251.2(MSH2):c.-225G>C
NM_000251.2(MSH2):c.-181G>A
NM_000251.2(MSH2):c.-81dupA
NM_000251.2(MSH2):c.-78_-77delTG
NM_000251.2(MSH2):c.1662-17dupG
NM_000179.2(MSH6):c.457+33_457+34insGTGT
NM_000179.2(MSH6):c.3173-16_3173-5delCCCTCTCTTTTA
NM_000179.2(MSH6):c.*15A>C
NM_000179.2(MSH6):c.*49_*68dupTTCAGACAACATTATGATCT
NM_001042492.2(NF1):c.-273A>C
NM_001042492.2(NF1):c.-272G>A
NM_001042492.2(NF1):c.60+9031_60+9035delAAGTT
NM_001042492.2(NF1):c.61-7486G>T
NM_001042492.2(NF1):c.288+2025T>G
NM_001042492.2(NF1):c.587-14T>A
NM_001042492.2(NF1):c.587-12T>A
NM_001042492.2(NF1):c.888+651T>A
NM_001042492.2(NF1):c.888+744A>G
NM_001042492.2(NF1):c.888+789A>G
NM_001042492.2(NF1):c.889-12T>A
NM_001042492.2(NF1):c.1260+1604A>G
NM_001042492.2(NF1):c.1261-19G>A
NM_001042492.2(NF1):c.1392+754T>G
NM_001042492.2(NF1):c.1393-592A>G
NM_001042492.2(NF1):c.1527+1159C>T
NM_001042492.2(NF1):c.1642-449A>G
NM_001128147.2(NF1):c.*481A>G
NM_001042492.2(NF1):c.2002-14C>G
NM_001042492.2(NF1):c.2252-11T>G
NM_001042492.2(NF1):c.2410-18C>G
NM_001042492.2(NF1):c.2410-16A>G
NM_001042492.2(NF1):c.2410-15A>G
NM_001042492.2(NF1):c.2410-12T>G
NM_001042492.2(NF1):c.2851-14_2851-13insA
NM_001042492.2(NF1):c.2991-11T>G
NM_001042492.2(NF1):c.3198-314G>A
NM_001042492.2(NF1):c.3974+260T>G
NM_001042492.2(NF1):c.4110+945A>G
NM_001042492.2(NF1):c.4173+278A>G
NM_001042492.2(NF1):c.4578-20_4578-18delAAG
NM_001042492.2(NF1):c.4578-14T>G
NM_001042492.2(NF1):c.5269-38A>G
NM_001042492.2(NF1):c.5610-456G>T
NM_001042492.2(NF1):c.5812+332A>G
NM_001042492.2(NF1):c.5813-279A>G
NM_001042492.2(NF1):c.6428-11T>G

NM_001042492.2(NF1):c.6642+18A>G
NM_001042492.2(NF1):c.7190-12T>A
NM_001042492.2(NF1):c.7190-11_7190-10insGTTT
NM_001042492.2(NF1):c.7971-321C>G
NM_001042492.2(NF1):c.7971-17C>G
NM_001042492.2(NF1):c.8113+25A>T
NM_000535.5(PMS2):c.1145-31_1145-13delCTGACCCTCTTCTCCGTCC
NM_000535.5(PMS2):c.23+21_23+28delTCCGGTGT
NM_002834.3(PTPN11):c.934-59T>A
NR_001566.1(TERC):n.-22C>T
chr3:g.169482906-169482906
NR_001566.1(TERC):n.-100C>G
chr3:g.169483086-169483086
NM_198253.2(TERT):c.2383-15C>T
NM_198253.2(TERT):c.-57A>C
chr17:g.7571520-7571520
NM_000546.5(TP53):c.673-39G>A
NM_000546.5(TP53):c.97-11C>G
NM_000546.5(TP53):c.-29+1G>T

GLOSSARY OF USED ABBREVIATIONS:

AD = autosomal dominant
AF = allele fraction (proportion of reads with mutated DNA / all reads)
AR = autosomal recessive
CNV = copy number variation e.g. one exon or multiexon deletion or duplication
gnomAD = genome aggregation database (reference population database; >138,600 individuals)
gnomAD AC/AN = allele count/allele number in the genome aggregation database (gnomAD)
HEM = hemizygous
HET = heterozygous
HOM = homozygous
ID = rsID in dbSNP
MT = Mitochondria
MutationTaster = *in silico* prediction tools used to evaluate the significance of identified amino acid changes.
Nomenclature = HGVS nomenclature for a variant in the nucleotide and the predicted effect of a variant in the protein level
OMIM = Online Mendelian Inheritance in Man®
PolyPhen = *in silico* prediction tool used to evaluate the significance of amino acid changes.
POS = genomic position of the variant in the format of chromosome:position
SIFT = *in silico* prediction tool used to evaluate the significance of amino acid changes.