Patient name: example report
HN: 123456789
Date of birth: 02/01/1985
Sex: Male

Sample type: EDTA Blood
Specimen id: 12345678-1
Date of collection: 01/03/2022
Date of receive: 01/03/2022

Date of result: 28/04/2023
Physician order: Dr. Examplereport Test

RESULT : Positive

TEST INFORMATION

Cancer screening includes 92 genes as shown in the section “condition associated gene” below.

TEST RESULTS

One Likely pathogenic variant in MSH2 was identified in this individual. One Likely pathogenic variant in MSH6 was identified in this individual. No other variants of relevance to the indication were identified. Please see below for more detailed variant information.

VARIANTS FINDING

Gene	Transcript	Chromosome position	Variant	Allele State	Inheritance	Classification
MSH2	NM_000251.3	Chr2:47698092	p.?	Heterozygous	Dominant	Likely pathogenic
MSH6	NM_000179.3	Chr2:48027178	p.Gly686Valfs*50	Heterozygous	Dominant	Likely pathogenic

INTERPRETATION SUMMARY

Doctor’s interpretation

RECOMMENDATIONS

The interpretation of these results should be done in the context of a patient’s medical record and family history. Please note that interpretation and classification of the variants reported here may change over time. Please see a genetic counselor for services regarding the implications of these results in the context of understanding the implications of incidental findings, family planning and the informing of family members of potentially shared genetic outcomes.

Patient name: example report **HN:** 123456789

DETAILED GENETIC VARIANT INFORMATION

VARIANTS FINDING

MSH2 NM_000251.3

Gene summary
This locus is frequently mutated in hereditary nonpolyposis colon cancer (HNPCC). When cloned, it was discovered to be a human homolog of the E. coli mismatch repair gene mutS, consistent with the characteristic alterations in microsatellite sequences (RER+ phenotype) found in HNPCC. Two transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, Apr 2012]

Variants summary
The splice acceptor variant NM_000251.3(MSH2):c.1662-12_1677del (p.?) has not been reported previously as a pathogenic variant nor as a benign variant, to our knowledge. The p.? variant is novel (not in any individuals) in gnomAD All. The p.? variant is novel (not in any individuals) in 1kG All. This variant mutates a splice-acceptor sequence and is predicted to disrupt the reading frame, resulting in nonsense mediated decay. This variant results in the loss of an acceptor splice site for the clinically relevant transcript. This variant disrupts the acceptor splice site for an exon upstream from the last coding exon resulting in a frameshift mutation that is predicted to cause nonsense mediated decay. The gene MSH2 has a low rate of benign loss of function variants as indicated by a low upper bound of the observed/expected confidence interval 0.33. The p.? variant is a loss of function variant in the gene MSH2, which is intolerant of Loss of Function variants, as indicated by the presence of existing pathogenic loss of function variant NP_000242.1:p.P5Afs*77 and 759 others. For these reasons, this variant has been classified as Likely Pathogenic.

MSH6 NM_000179.3

Gene summary
This gene encodes a member of the DNA mismatch repair MutS family. In E. coli, the MutS protein helps in the recognition of mismatched nucleotides prior to their repair. A highly conserved region of approximately 150 aa, called the Walker-A adenine nucleotide binding motif, exists in MutS homologs. The encoded protein heterodimerizes with MSH2 to form a mismatch recognition complex that functions as a bidirectional molecular switch that exchanges ADP and ATP as DNA mismatches are bound and dissociated. Mutations in this gene may be associated with hereditary nonpolyposis colon cancer, colorectal cancer, and endometrial cancer. Transcripts variants encoding different isoforms have been described. [provided by RefSeq, Jul 2013]

Variants summary
The frameshift deletion NM_000179.3(MSH6):c.2057delG (p.Gly686Valfs*50) has not been reported previously as a pathogenic variant nor as a benign variant, to our knowledge. The p.Gly686Valfs*50 variant is novel (not in any individuals) in gnomAD All. The p.Gly686Valfs*50 variant is novel (not in any individuals) in 1kG All. This variant is predicted to cause loss of normal protein function through protein truncation caused a frameshift mutation. The frame shifted sequence continues 50 residues until a stop codon is reached. This variant is a frameshift variant which occurs in an exon of MSH6 upstream of where nonsense mediated decay is predicted to occur. This variant has been previously classified as pathogenic, indicating that the region is critical to protein function. There are 567 downstream pathogenic loss of function variants, with the furthest variant being 651 residues downstream of this variant. This indicates that the region is critical to protein function. The p.Gly686Valfs*50 variant is a loss of function variant in the gene MSH6, which is intolerant of Loss of Function variants, as indicated by the presence of existing pathogenic loss of function variant NP_000170.1:p.M1Ifs*17 and 817 others. For these reasons, this variant has been classified as Likely Pathogenic.

Patient name: example report **HN:** 123456789

METHODOLOGY

Genomic DNA is extracted from an individual at Bumrungrad Hospital. DNA sample is sent to the Macrogen, Korea to process Whole Exome Sequencing (WES). Library preparation, clustering and sequencing are processed on the Illumina platform to cover the coding regions of targeted genes ± ~10 bases of non-coding DNA flanking each exon. Raw data in an average at 6 Gb were generated. Reads from the sequence output were aligned to the human reference genome (GRCh37) using BWA. Variants are called using GATK pipeline. The tertiary analysis is performed at Bumrungrad Hospital. The variants were annotated and filtered using the Golden Helix VarSeq analysis workflow implementing the ACMG guidelines for the interpretation of sequence variants. This includes a comparison against the gnomAD population catalog of variants in 123,136 exomes, the 1000 Genomes Project Consortium's publication of 2,500 genomes, the NCBI ClinVar database of clinical assertions on variant's pathogenicity and multiple lines of computational evidence on conservation and functional impact.

Coverage Statistics for cancer screen panel

Target region / Coverage	WES Target region	Cancer panel target region
Mean depth (X)	**54.8X**	**53.7X**
Mean depth ≥ 10X	**95.1%**	**96.7%**

VARIANT ASSESSMENT PROCESS

The following databases and in-silico algorithms are used to annotate and evaluate the impact of the variant in the context of human disease: 1000 genomes, gnomAD, ClinVar, OMIM, dbSNP, NCIB RefSeq Genes, ExAC Gene Constraints, VS-SIFT, VS-PolyPhen2, PhyloP, GERP++, GeneSplicer, MaxEntScan, NNSplice, PWM Splice Predictor. Analysis was reported using the to HGVS nomenclature (www.hgvs.org/mutnomen) as implemented by the VarSeq transcript annotation algorithm. The reported transcript matches that used most frequently by the clinical labs submitting to ClinVar.

LIMITATIONS

It should be noted that the test result is limited to a set of genes indicated in the panel and might not cover all possible variants related to the particular condition. For some target regions, the depth covered for analysis may be variable. However, any targeted gene that fails to meet the acceptance criteria (Mean depth **≥** 10X) will be noted. Due to these limitations, ruling out the diagnosis of a genetic disorder should not be made based on negative results. An evaluation by alternative methods should be considered if a specific clinical disorder is suspected. This report only includes variants that meet a level of evidence threshold for cause or contribute to disease/condition. Reported variants are not confirmed by Sanger sequencing. Certain classes of genomic variants are also not covered using the NGS testing technology, including repeat expansions, large deletion or large duplication (≥50 kb), translocations and gene fusions or other complex structural rearrangements.

Patient name: example report **HN:** 123456789

DISCLAIMER

The result interpretation is based on the most current scientific and analytical standards. However, more evidence for disease association of genes and causal pathogenic variants are discovered every year, and it is recommended that genetic variants are re-interpreted with updated software and annotations periodically. There is also a possibility of an error in the result due to contaminants in the sample, rare technical errors, a rare genetic variant that could interfere with the analysis. This test should be used in compliance with the other diagnostic test. Note that this test cannot exclude the possibility of variants in genes not analyzed or assayed with incomplete coverage. Even though this test is not designed to distinguish between somatic and germline variants, if variant of somatic is detected, supplementary testing may be compulsory to clarify the significance of results. Genetic counseling is recommended to help understand the test result and explain the implications of this result for the patients and other family members. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary.

Patient name: example report **HN:** 123456789

CONDITION ASSOCIATED GENE

The table shows the list of 92 genes related to cancer conditions analyzed in this test. Gene-Phenotype relationship information is retrieved from http:/www.omim.org.

Gene	Transcript	Gene MIM number	Gene associated condition
AIP	NM_003977.4	605555	Pituitary adenoma
ALK	NM_004304.5	105590	Neuroblastoma
APC	NM_000038.6	611731	Familial adenomatous polyposis, Gardner syndrome, Brain tumor-polyposis syndrome, Desmoid disease, Gastric adenocarcinoma and proximal polyposis of the stomach
ATM	NM_000051.4	607585	Ataxia-telangiectasia, Breast cancer
AXIN2	NM_004655.4	604025	Oligodontia-colorectal cancer syndrome
BAP1	NM_004656.4	603089	BAP1 tumor predisposition syndrome
BARD1	NM_000465.4	601593	Breast cancer
BLM	NM_000057.4	604610	Bloom syndrome
BMPR1A	NM_004329.3	601299	Hereditary mixed polyposis syndrome, Juvenile polyposis syndrome
BRCA1	NM_007294.4	113705	Fanconi anemia, Familial breast-ovarian cancer, Pancreatic cancer
BRCA2	NM_000059.4	600185	Fanconi anemia, Wilms tumor, Familial breast-ovarian cancer, Glioblastoma, Medulloblastoma, Pancreatic cancer, Prostate cancer
BRIP1	NM_032043.3	605882	Fanconi anemia, Breast cancer
CDC73	NM_024529.5	607393	Hyperparathyroidism jaw tumour syndrome, Parathyroid carcinoma
CDH1	NM_004360.5	192090	Diffuse gastric cancer, breast cancer, Prostate cancer
CDK4	NM_000075.4	123829	Cutaneous melanoma
CDKN1B	NM_004064.5	600778	Multiple endocrine neoplasia,
CDKN1C	NM_000076.2	600856	Beckwith-Wiedemann syndrome
CDKN2A	NM_000077.5	600160	Melanoma and neural system tumor syndrome, Cutaneous melanoma, Familial atypical multiple mole melanoma-pancreatic carcinoma syndrome
CEBPA	NM_004364.5	116897	Acute myeloid Leukemia
CHEK2	NM_007194.4	604373	Li-Fraumeni syndrome, Breast cancer, Colorectal cancer, Prostate cancer
CYLD	NM_015247.3	605018	Brooke-Spiegler syndrome, Familial cylindromatosis, Multiple familial trichoepithelioma
DICER1	NM_177438.3	606241	Multinodular goiters, Pleuropulmonary blastoma, Embryonal rhabdomyosarcoma
DIS3L2	NM_152383.5	614184	Perlman syndrome
EGFR	NM_005228.5	131550	Lung cancer
EPCAM	NM_002354.3	185535	Hereditary nonpolyposis colorectal cancer (Lynch syndrome)
EXT1	NM_000127.3	608177	Chondrosarcoma, Hereditary multiple osteochondromas
EXT2	NM_207122.2	608210	Hereditary multiple osteochondromas
FANCA	NM_000135.4	607139	Fanconi anemia
FANCC	NM_000136.3	613899	Fanconi anemia
FH	NM_000143.4	136850	Hereditary leiomyomatosis and renal cell cancer
FLCN	NM_144997.7	607273	Birt-Hogg-Dube syndrome
GALNT12	NM_024642.5	610290	Colorectal cancer

Patient name: example report **HN**: 123456789

Gene	Transcript	Gene MIM number	Gene associated condition
GATA2	NM_032638.5	137295	Acute myeloid leukemia, Myelodysplastic syndrome
GPC3	NM_004484.4	300037	Simpson-Golabi-Behmel syndrome
GREM1	NM_013372.7	603054	Hereditary mixed polyposis syndrome
HOXB13	NM_006361.6	604607	Prostate cancer
HRAS	NM_005343.4	190020	Costello syndrome
KIT	NM_000222.3	164920	Gastrointestinal stromal tumor, Cutaneous mastocytosis, Piebaldism
LZTR1	NM_006767.4	600574	Schwannomatosis
MAX	NM_002382.5	154950	Pheochromocytoma
MEN1	NM_130799.2	613733	Multiple endocrine neoplasia
MET	NM_001127500.3	164860	Papillary Renal Cell Carcinoma, Osteofibrous dysplasia
MITF	NM_000248.4	156845	Cutaneous melanoma
MLH1	NM_000249.4	120436	Hereditary nonpolyposis colorectal cancer (Lynch syndrome), Mismatch repair cancer syndrome, Muir-Torre syndrome
MLH3	NM_001040108.2	604395	Hereditary nonpolyposis colorectal cancer (Lynch syndrome), Endometrial cancer
MRE11	NM_005591.4	600814	Ataxia-telangiectasia
MSH2	NM_000251.3	609309	Hereditary nonpolyposis colorectal cancer (Lynch syndrome), Mismatch repair cancer syndrome, Muir-Torre syndrome
MSH3	NM_002439.5	600887	Familial adenomatous polyposis
MSH6	NM_000179.3	600678	Hereditary nonpolyposis colorectal cancer (Lynch syndrome), Mismatch repair cancer syndrome, Endometrial cancers
MUTYH	NM_001128425.2	604933	Familial adenomatous polyposis
NBN	NM_002485.5	602667	Aplastic anemia, Acute lymphoblastic leukemia, Nijmegen breakage syndrome
NF1	NM_000267.3	613113	Juvenile myelomonocytic leukemia, Familial spinal neurofibromatosis sacroma, Neurofibromatosis
NF2	NM_000268.4	607379	Neurofibromatosis
NTHL1	NM_002528.7	602656	Familial adenomatous polyposis
PALB2	NM_024675.4	610355	Fanconi anemia, Breast cancer, Pancreatic cancer
PDGFRA	NM_006206.6	173490	GIST-plus syndrome
PHOX2B	NM_003924.4	603851	Neuroblastoma
PMS2	NM_000535.7	600259	Hereditary nonpolyposis colorectal cancer (Lynch syndrome), Mismatch repair cancer syndrome
POLD1	NM_002691.4	174761	Colorectal cancer
POLE	NM_006231.4	174762	Colorectal cancer
POT1	NM_015450.3	606478	Glioma, Cutaneous melanoma
PRKAR1A	NM_002734.5	188830	Carney complex
PTCH1	NM_000264.5	601309	Basal cell nevus syndrome
PTEN	NM_000314.8	601728	Cowden syndrome, Glioma, Meningioma
RAD51C	NM_058216.3	602774	Fanconi anemia, Familial breast-ovarian cancer
RAD51D	NM_002878.4	602954	Familial breast-ovarian cancer
RB1	NM_000321.3	614041	Retinoblastoma

Patient name: example report **HN**: 123456789

Gene	Transcript	Gene MIM number	Gene associated condition
RECQL4	NM_004260.4	603780	Baller-Gerold syndrome, RAPADILINO syndrome, Rothmund-Thomson syndrome
RET	NM_020975.6	164761	Medullary thyroid carcinoma, Multiple endocrine neoplasia, Pheochromocytoma
RNF43	NM_017763.6	612482	Sessile serrated polyposis cancer syndrome
RUNX1	NM_001754.5	151385	Acute myeloid Leukemia, Familial platelet disorder with associated myeloid malignancy
SDHA	NM_004168.4	600857	Paragangliomas
SDHAF2	NM_017841.4	613019	Paragangliomas
SDHB	NM_003000.3	185470	Gastrointestinal stromal tumor, Paraganglioma and gastric stromal sarcoma, Paragangliomas, Pheochromocytoma
SDHC	NM_003001.5	602413	Gastrointestinal stromal tumor, Paraganglioma and gastric stromal sarcoma, Paragangliomas,
SDHD	NM_003002.4	602690	Paraganglioma and gastric stromal sarcoma, Pheochromocytoma
SMAD4	NM_005359.6	600993	Juvenile polyposis/hereditary hemorrhagic telangiectasia syndrome, Myhre syndrome, Juvenile polyposis syndrome
SMARCA4	NM_001128849.3	603254	Rhabdoid tumor predisposition syndrome
SMARCB1	NM_003073.5	601607	Rhabdoid tumor predisposition syndrome, Schwannomatosis
SMARCE1	NM_003079.5	603111	Meningioma
STK11	NM_000455.5	602216	Peutz-Jeghers syndrome
SUFU	NM_016169.4	607035	Basal cell nevus syndrome, Medulloblastoma, Meningioma
TERC	NR_001566.1	602322	Dyskeratosis congenita, Telomere-related pulmonary fibrosis and/or bone marrow failure
TERT	NM_198253.3	187270	Dyskeratosis congenita, Telomere-related pulmonary fibrosis and/or bone marrow failure, Acute myeloid leukemia, Cutaneous melanoma
TMEM127	NM_017849.4	613403	Pheochromocytoma
TP53	NM_000546.6	191170	Adrenocortical carcinoma, Basal cell carcinoma, Li-Fraumeni syndrome, Choroid plexus papilloma, Colorectal cancer, Glioma
TSC1	NM_000368.5	605284	Tuberous sclerosis
TSC2	NM_000548.5	191092	Tuberous sclerosis
VHL	NM_000551.4	608537	Pheochromocytoma, von Hippel-Lindau syndrome
WRN	NM_000553.6	604611	Werner syndrome
WT1	NM_024426.6	607102	Wilms tumor
XRCC2	NM_005431.2	600375	Fanconi anemia

Prepared by: Srichan Bunlungsup, Ph.D.

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Approved by: Asst.Prof. Dr. Polakit Teekakirikul, M.D.

Bumrungrad International HOSPITAL

Cardio screening panel

Patient name: example report
HN: 123456789
Date of birth: 02/01/1985
Sex: Male

Sample type: EDTA Blood
Specimen id: 12345678-1
Date of collection: 01/03/2022
Date of receive: 01/03/2022

Date of result: 28/04/2023
Physician order: Dr. Examplereport Test

RESULT : Negative

TEST INFORMATION

Cardio screening includes 98 genes as shown in the section “condition associated gene” below.

TEST RESULTS

No genetic variant with clinical significance is found.

INTERPRETATION SUMMARY

There were no known, clinically significant genetic changes detected that confer a genetic predisposition to, or carrier status for, certain types of heart conditions in this panel. Please refer to the complete list of genes and conditions below. Please also note that other risks based on non-genetic factors or other genetic causes not evaluated with this test may still be of clinical significance.

RECOMMENDATIONS

The interpretation of these results should be done in the context of a patient’s medical record and family history. Please note that interpretation and classification of the variants reported here may change over time. Please see a genetic counselor for services regarding the implications of these results in the context of understanding the implications of incidental findings, family planning and the informing of family members of potentially shared genetic outcomes.

Patient name: example report **HN:** 123456789

METHODOLOGY

Genomic DNA is extracted from an individual at Bumrungrad Hospital. DNA sample is sent to the Macrogen, Korea to process Whole Exome Sequencing (WES). Library preparation, clustering and sequencing are processed on the Illumina platform to cover the coding regions of targeted genes ± ~10 bases of non-coding DNA flanking each exon. Raw data in an average at 6 Gb were generated. Reads from the sequence output were aligned to the human reference genome (GRCh37) using BWA. Variants are called using GATK pipeline. The tertiary analysis is performed at Bumrungrad Hospital. The variants were annotated and filtered using the Golden Helix VarSeq analysis workflow implementing the ACMG guidelines for the interpretation of sequence variants. This includes a comparison against the gnomAD population catalog of variants in 123,136 exomes, the 1000 Genomes Project Consortium's publication of 2,500 genomes, the NCBI ClinVar database of clinical assertions on variant's pathogenicity and multiple lines of computational evidence on conservation and functional impact.

Coverage Statistics for cardio screen panel

Target region / Coverage	WES Target region	Cardio panel target region
Mean depth (X)	**54.8X**	**53.7X**
Mean depth ≥ 10X	**95.1%**	**96.7%**

VARIANT ASSESSMENT PROCESS

The following databases and in-silico algorithms are used to annotate and evaluate the impact of the variant in the context of human disease: 1000 genomes, gnomAD, ClinVar, OMIM, dbSNP, NCIB RefSeq Genes, ExAC Gene Constraints, VS-SIFT, VS-PolyPhen2, PhyloP, GERP++, GeneSplicer, MaxEntScan, NNSplice, PWM Splice Predictor. Analysis was reported using the to HGVS nomenclature (www.hgvs.org/mutnomen) as implemented by the VarSeq transcript annotation algorithm. The reported transcript matches that used most frequently by the clinical labs submitting to ClinVar.

LIMITATIONS

It should be noted that the test result is limited to a set of genes indicated in the panel and might not cover all possible variants related to the particular condition. For some target regions, the depth covered for analysis may be variable. However, any targeted gene that fails to meet the acceptance criteria (Mean depth ≥ 10X) will be noted. Due to these limitations, ruling out the diagnosis of a genetic disorder should not be made based on negative results. An evaluation by alternative methods should be considered if a specific clinical disorder is suspected. This report only includes variants that meet a level of evidence threshold for cause or contribute to disease/condition. Reported variants are not confirmed by Sanger sequencing. Certain classes of genomic variants are also not covered using the NGS testing technology, including repeat expansions, large deletion or large duplication (≥50 kb), translocations and gene fusions or other complex structural rearrangements.

Patient name: example report **HN:** 123456789

DISCLAIMER

The result interpretation is based on the most current scientific and analytical standards. However, more evidence for disease association of genes and causal pathogenic variants are discovered every year, and it is recommended that genetic variants are re-interpreted with updated software and annotations periodically. There is also a possibility of an error in the result due to contaminants in the sample, rare technical errors, a rare genetic variant that could interfere with the analysis. This test should be used in compliance with the other diagnostic test. Note that this test cannot exclude the possibility of variants in genes not analyzed or assayed with incomplete coverage. Even though this test is not designed to distinguish between somatic and germline variants, if variant of somatic is detected, supplementary testing may be compulsory to clarify the significance of results. Genetic counseling is recommended to help understand the test result and explain the implications of this result for the patients and other family members. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary.

Patient name: example report **HN:** 123456789

CONDITION ASSOCIATED GENE

The table shows the list of 98 genes related to cardiovascular conditions analyzed in this test. Gene-Phenotype relationship information is retrieved from http:/www.omim.org.

Gene	Transcript	Gene MIM number	Gene associated condition
ACTA2	NM_001613.4	102620	Aortic aneurysm, Familial thoracic 6, Moyamoya disease 5, Multisystemic smooth muscle dysfunction syndrome
ACTC1	NM_005159.5	102540	Atrial septal defect, Dilated cardiomyopathy, Hypertrophic cardiomyopathy, Left ventricular noncompaction
ACTN2	NM_001103.4	102573	Dilated cardiomyopathy, Hypertrophic cardiomyopathy, Distal Myopathy
ACVRL1	NM_000020.3	601284	Hereditary hemorrhagic telangiectasia
ANKRD1	NM_014391.3	609599	Dilated cardiomyopathy
APOB	NM_000384.3	107730	Hypercholesterolemia, Hypobetalipoproteinemia
BAG3	NM_004281.4	603883	Dilated cardiomyopathy, Myofibrillar myopathy
BMPR2	NM_001204.7	600799	Pulmonary hypertension, Pulmonary veno-occlusive disease
CACNA1C	NM_000719.7	114205	Brugada syndrome, Long QT syndrome, Timothy syndrome
CACNB2	NM_201590.3	600003	Brugada syndrome
CALM1	NM_006888.6	114180	Long QT syndrome, Catecholaminergic polymorphic ventricular tachycardia
CALM2	NM_001743.6	114182	Long QT syndrome
CALM3	NM_005184.4	114183	Catecholaminergic polymorphic ventricular tachycardia, Long QT syndrome
CASQ2	NM_001232.4	114251	Catecholaminergic polymorphic ventricular tachycardia
CAV1	NM_001753.5	601047	Primary pulmonary hypertension
CAV3	NM_033337.3	601253	Hypertrophic cardiomyopathy, Long QT syndrome, Distal Myopathy
COL3A1	NM_000090.4	120180	Vascular Ehlers-Danlos syndrome
CRYAB	NM_001885.3	123590	Dilated cardiomyopathy, Myofibrillar Myopathy
CSRP3	NM_003476.5	600824	Dilated cardiomyopathy, Hypertrophic cardiomyopathy
DES	NM_001927.4	125660	Dilated cardiomyopathy, Myofibrillar Myopathy
DMD	NM_004006.3	300377	Dilated cardiomyopathy, Muscular dystrophy
DSC2	NM_024422.6	125645	Arrhythmogenic right ventricular Cardiomyopathy
DSG2	NM_001943.5	125671	Arrhythmogenic right ventricular Cardiomyopathy, Dilated cardiomyopathy
DSP	NM_004415.4	125647	Arrhythmogenic right ventricular Cardiomyopathy, Dilated cardiomyopathy
DTNA	NM_001390.4	601239	Left ventricular noncompaction
EMD	NM_000117.3	300384	Muscular dystrophy
ENG	NM_000118.3	131195	Hereditary hemorrhagic telangiectasia
EYA4	NM_004100.5	603550	Dilated cardiomyopathy
F2	NM_000506.5	176930	Prothrombin deficiency, Thrombophilia
F5	NM_000130.5	612309	Factor V deficiency, Thrombophilia
F9	NM_000133.4	300746	Hemophilia, Thrombophilia
FBN1	NM_000138.5	134797	Geleophysic dysplasia, Marfan syndrome, MASS syndrome,Weill-Marchesani syndrome
FHL1	NM_001449.5	300163	Uruguay faciocardiomusculoskeletal syndrome, Muscular dystrophy
FKTN	NM_001079802.2	607440	Dilated cardiomyopathy, Muscular dystrophy

Patient name: example report **HN:** 123456789

Gene	Transcript	Gene MIM number	Gene associated condition
FLNC	NM_001458.5	102565	Hypertrophic cardiomyopathy, Familial restrictive cardiomyopathy, Distal myopathy, Myofibrillar myopathy
GATAD1	NM_021167.5	614518	Dilated cardiomyopathy
GDF2	NM_016204.4	605120	Hereditary hemorrhagic telangiectasia
GLA	NM_000169.3	300644	Fabry disease
GPD1L	NM_015141.4	611778	Brugada syndrome
HCN4	NM_005477.3	605206	Brugada syndrome, Sick sinus syndrome
JPH2	NM_020433.5	605267	Dilated cardiomyopathy, Hypertrophic cardiomyopathy
JUP	NM_002230.4	173325	Arrhythmogenic right ventricular cardiomyopathy, Naxos disease
KCNE1	NM_000219.6	176261	Jervell and Lange-Nielsen syndrome, Long QT syndrome
KCNE2	NM_172201.2	603796	Familial atrial fibrillation, Long QT syndrome
KCNH2	NM_000238.4	152427	Long QT syndrome, Short QT syndrome
KCNJ2	NM_000891.3	600681	Andersen syndrome, Familial atrial fibrillation, Short QT syndrome
KCNQ1	NM_000218.3	607542	Familial atrial fibrillation, Jervell and Lange-Nielsen syndrome, Long QT syndrome
LAMA4	NM_002290.5	600133	Dilated cardiomyopathy
LAMP2	NM_002294.3	309060	Danon disease
LDB3	NM_007078.3	605906	Dilated cardiomyopathy, Hypertrophic cardiomyopathy, Left ventricular noncompaction, Myofibrillar myopathy
LDLR	NM_000527.5	606945	Familial Hypercholesterolemia
LDLRAP1	NM_015627.3	605747	Familial Hypercholesterolemia
LMNA	NM_170707.4	150330	Dilated cardiomyopathy, Muscular dystrophy, Heart-hand syndrome, Hutchinson-Gilford progeria syndrome, Familial partial lipodystrophy, Malouf syndrome
MAP2K1	NM_002755.4	176872	Cardiofaciocutaneous syndrome
MAP2K2	NM_030662.4	601263	Cardiofaciocutaneous syndrome
MYBPC3	NM_000256.3	600958	Dilated cardiomyopathy, Hypertrophic cardiomyopathy, Left ventricular noncompaction
MYH11	NM_002474.3	160745	Familial thoracic aortic aneurysm and dissection
MYH6	NM_002471.4	160710	Atrial septal defect, Dilated cardiomyopathy, Hypertrophic cardiomyopathy, Sick sinus syndrome
MYH7	NM_000257.4	160760	Dilated cardiomyopathy, Hypertrophic cardiomyopathy, Distal myopathy, Left ventricular noncompaction, Myopathy
MYL2	NM_000432.4	160781	Cardiomyopathy, Myofibrillar myopathy
MYL3	NM_000258.3	160790	Hypertrophic cardiomyopathy
MYLK	NM_053025.4	600922	Familial thoracic aortic aneurysm and dissection
MYLK2	NM_033118.4	606566	Hypertrophic cardiomyopathy
MYOZ2	NM_016599.5	605602	Hypertrophic cardiomyopathy
MYPN	NM_032578.4	608517	Dilated cardiomyopathy, Familial restrictive cardiomyopathy, Hypertrophic cardio, Myopathy
NEXN	NM_144573.4	613121	Dilated cardiomyopathy, Hypertrophic cardiomyopathy
NKX2-5	NM_004387.4	600584	Atrial septal defect, Conotruncal heart malformations, Hypoplastic left heart syndrome, Tetralogy of Fallot, Ventricular septal defect
PCSK9	NM_174936.4	607786	Familial hypercholesterolemia
PKP2	NM_004572.4	602861	Arrhythmogenic right ventricular cardiomyopathy
PLN	NM_002667.5	172405	Dilated cardiomyopathy, Hypertrophic cardiomyopathy
PRKAG2	NM_016203.4	602743	Hypertrophic cardiomyopathy, Lethal congenital glycogen storage disease of the heart, Wolff-Parkinson-White syndrome
PRKG1	NM_006258.4	176894	Familial thoracic aortic aneurysm and dissection

Patient name: example report **HN:** 123456789

Gene	Transcript	Gene MIM number	Gene associated condition
PROC	NM_000312.4	612283	Thrombophilia
PROS1	NM_000313.4	176880	Thrombophilia
RAF1	NM_002880.4	164760	Dilated cardiomyopathy, LEOPARD syndrome, Noonan syndrome
RBM20	NM_001134363.3	613171	Dilated cardiomyopathy
RYR2	NM_001035.3	180902	Arrhythmogenic right ventricular Cardiomyopathy, Ventricular arrhythmias, Catecholaminergic polymorphic ventricular tachycardia
SCN5A	NM_198056.3	600163	Familial atrial fibrillation, Brugada syndrome, Dilated cardiomyopathy, Progressive familial heart block, Long QT syndrome, Sick sinus syndrome, Familial ventricular fibrillation
SERPINC1	NM_000488.4	107300	Thrombophilia
SGCD	NM_000337.6	601411	Dilated cardiomyopathy, Muscular dystrophy
SMAD3	NM_005902.4	603109	Loeys-Dietz syndrome
SMAD4	NM_005359.6	600993	Hereditary hemorrhagic telangiectasia
TAZ	NM_000116.5	300394	Barth syndrome
TCAP	NM_003673.4	604488	Hypertrophic cardiomyopathy, Dilated cardiomyopathy, Muscular dystrophy
TGFB2	NM_003238.6	190220	Loeys-Dietz syndrome
TGFB3	NM_003239.5	190230	Arrhythmogenic right centricular cardiomyopathy, Loeys-Dietz syndrome
TGFBR1	NM_004612.4	190181	Loeys-Dietz syndrome
TGFBR2	NM_003242.6	190182	Loeys-Dietz syndrome
TMEM43	NM_024334.3	612048	Arrhythmogenic right ventricular cardiomyopathy, Muscular dystrophy
TMPO	NM_003276.2	188380	Dilated cardiomyopathy
TNNC1	NM_003280.3	191040	Dilated cardiomyopathy, Hypertrophic cardiomyopathy
TNNI3	NM_000363.5	191044	Dilated cardiomyopathy, Hypertrophic cardiomyopathy, Familial restrictive cardiomyopathy
TNNT2	NM_001001430.3	191045	Dilated cardiomyopathy, Familial restrictive cardiomyopathy, Hypertrophic cardiomyopathy, Left ventricular noncompaction
TPM1	NM_001018005.2	191010	Dilated cardiomyopathy, Hypertrophic cardiomyopathy, Left ventricular noncompaction
TRDN	NM_006073.4	603283	Cardiac arrhythmia syndrome
TTN	NM_001267550.2	188840	Dilated cardiomyopathy, Hypertrophic cardiomyopathy, Muscular dystrophy, Myofibrillar myopathy
TTR	NM_000371.4	176300	Hereditary transthyretin(TTR)-related amyloidosis
VCL	NM_014000.3	193065	Dilated cardiomyopathy, Hypertrophic cardiomyopathy

Prepared by: Srichan Bunlungsup, Ph.D.

Reviewed by: Wipa Panmontha, Ph.D.

Approved by: Asst.Prof. Dr. Polakit Teekakirikul, M.D.

Patient name: example report
HN: 123456789
Date of birth: 02/01/1985
Sex: Male

Sample type: EDTA Blood
Specimen id: 12345678-1
Date of collection: 01/03/2022
Date of receive: 01/03/2022

Date of result: 28/04/2023
Physician order: Dr. Examplereport Test

RESULT : Negative

TEST INFORMATION

Additional finding includes 14 genes as shown in the section “condition associated gene” below.

TEST RESULTS

No genetic variant with clinical significance is found.

INTERPRETATION SUMMARY

There were no known, clinically significant genetic changes detected that confer a genetic predisposition to, or carrier status for, certain types of actionable medical genetic conditions analyzed in this panel. Please refer to the complete list of genes and conditions below. Please also note that other risks based on non-genetic factors or other genetic causes not evaluated with this test may still be of clinical significance.

RECOMMENDATIONS

The interpretation of these results should be done in the context of a patient’s medical record and family history. Please note that interpretation and classification of the variants reported here may change over time. Please see a genetic counselor for services regarding the implications of these results in the context of understanding the implications of incidental findings, family planning and the informing of family members of potentially shared genetic outcomes.

Patient name: example report **HN:** 123456789

METHODOLOGY

Genomic DNA is extracted from an individual at Bumrungrad Hospital. DNA sample is sent to the Macrogen, Korea to process Whole Exome Sequencing (WES). Library preparation, clustering and sequencing are processed on the Illumina platform to cover the coding regions of targeted genes ± ~10 bases of non-coding DNA flanking each exon. Raw data in an average at 6 Gb were generated. Reads from the sequence output were aligned to the human reference genome (GRCh37) using BWA. Variants are called using GATK pipeline. The tertiary analysis is performed at Bumrungrad Hospital. The variants were annotated and filtered using the Golden Helix VarSeq analysis workflow implementing the ACMG guidelines for the interpretation of sequence variants. This includes a comparison against the gnomAD population catalog of variants in 123,136 exomes, the 1000 Genomes Project Consortium's publication of 2,500 genomes, the NCBI ClinVar database of clinical assertions on variant's pathogenicity and multiple lines of computational evidence on conservation and functional impact.

Coverage Statistics for additional finding

Target region / Coverage	WES Target region	Additional finding target region
Mean depth (X)	**54.8X**	**53.7X**
Mean depth ≥ 10X	**95.1%**	**96.7%**

VARIANT ASSESSMENT PROCESS

The following databases and in-silico algorithms are used to annotate and evaluate the impact of the variant in the context of human disease: 1000 genomes, gnomAD, ClinVar, OMIM, dbSNP, NCIB RefSeq Genes, ExAC Gene Constraints, VS-SIFT, VS-PolyPhen2, PhyloP, GERP++, GeneSplicer, MaxEntScan, NNSplice, PWM Splice Predictor. Analysis was reported using the to HGVS nomenclature (www.hgvs.org/mutnomen) as implemented by the VarSeq transcript annotation algorithm. The reported transcript matches that used most frequently by the clinical labs submitting to ClinVar.

LIMITATIONS

It should be noted that the test result is limited to a set of genes indicated in the panel and might not cover all possible variants related to the particular condition. For some target regions, the depth covered for analysis may be variable. However, any targeted gene that fails to meet the acceptance criteria (Mean depth ≥ 10X) will be noted. Due to these limitations, ruling out the diagnosis of a genetic disorder should not be made based on negative results. An evaluation by alternative methods should be considered if a specific clinical disorder is suspected. This report only includes variants that meet a level of evidence threshold for cause or contribute to disease/condition. Reported variants are not confirmed by Sanger sequencing. Certain classes of genomic variants are also not covered using the NGS testing technology, including repeat expansions, large deletion or large duplication (≥50 kb), translocations and gene fusions or other complex structural rearrangements.

Patient name: example report **HN:** 123456789

DISCLAIMER

The result interpretation is based on the most current scientific and analytical standards ·However, more evidence for disease association of genes and causal pathogenic variants are discovered every year, and it is recommended that genetic variants are re-interpreted with updated software and annotations periodically ·There is also a possibility of an error in the result due to contaminants in the sample, rare technical errors, a rare genetic variant that could interfere with the analysis ·This test should be used in compliance with the other diagnostic test ·Note that this test cannot exclude the possibility of variants in genes not analyzed or assayed with incomplete coverage ·Even though this test is not designed to distinguish between somatic and germline variants, if variant of somatic is detected, supplementary testing may be compulsory to clarify the significance of results ·Genetic counseling is recommended to help understand the test result and explain the implications of this result for the patients and other family members ·This test has not been cleared or approved by the U·S ·Food and Drug Administration)FDA ·(The FDA has determined that such clearance or approval is not necessary·

Patient name: example report **HN:** 123456789

CONDITION ASSOCIATED GENE

The table shows the list of 14 genes related to additional conditions analyzed in this test. Gene-Phenotype relationship information is retrieved from http:/www.omim.org

Gene	Transcript	Gene MIM number	Gene associated condition
ATP7B	NM_000053.4	606882	Wilson disease
BTD	NM_001370658.1	609019	Biotinidase deficiency
CACNA1S	NM_000069.3	114208	Malignant hyperthermia
GAA	NM_000152.5	606800	Pompe disease
HAMP	NM_021175.4	606464	Hereditary hemochromatosis
HFE	NM_000410.4	613609	Hereditary hemochromatosis
HJV	NM_213653.4	608374	Hereditary hemochromatosis
HNF1A	NM_000545.8	142410	Maturity-Onset of Diabetes of the Young
OTC	NM_000531.6	300461	Ornithine transcarbamylase deficiency
RPE65	NM_000329.3	180069	RPE65-related retinopathy
RYR1	NM_000540.3	180901	Malignant hyperthermia
SERPINA1	NM_000295.5	107400	Alpha-1-antitrypsin deficiency
SLC40A1	NM_014585.6	604653	Hereditary hemochromatosis
TFR2	NM_003227.4	604720	Hereditary hemochromatosis

Prepared by: Srichan Bunlungsup, Ph.D.

Reviewed by: Wipa Panmontha, Ph.D.

Approved by: Asst.Prof. Dr. Polakit Teekakirikul, M.D.

Patient name: example report
HN: 123456789
Date of birth: 02/01/1985
Sex: Male

Sample type: EDTA Blood
Specimen id: 12345678-1
Date of collection: 01/03/2022
Date of receive: 01/03/2022

Date of result: 28/04/2023
Physician order: Dr. Examplereport Test

RESULT : Positive

TEST INFORMATION

Pharmacogenomics finding includes 2 genes: CACNA1S and RYR1, as shown in the section "condition associated gene" below.

TEST RESULTS

An Individual heterozygous or homozygous for CACNA1S and/or RYR1 Malignant Hyperthermia (MH)-causative variant as designated by the European Malignant Hyperthermia Group (EMHG).

VARIANTS FINDING

Gene	Transcript	Chromosome position	Variant	Allele State	Inheritance	Classification
CACNA1S	NM_000069.3	Chr1:201061121	p.Arg174Trp	Heterozygous	Dominant	Likely pathogenic
RYR1	NM_000540.3	Chr19: 38937350	p.G248R	Heterozygous	Dominant	Pathogenic

INTERPRETATION SUMMARY

Individuals are at increased risk of developing malignant hyperthermia if administered potent volatile anesthetics ((desflurane (suprane®), enflurane, ether, halothane, isoflurane, methoxyflurane (penthrox®) and sevoflurane)) or the depolarizing muscle relaxant succinylcholine (also known as suxamethonium).

RECOMMENDATIONS

Halogenated volatile anesthetics or depolarizing muscle relaxants succinylcholine are relatively contraindicated in persons with Malignant Hyperthermia Susceptibility. They should not be used, except in extraordinary circumstances in which the benefits outweigh the risks. In general, alternative anesthetics are widely available and effective in patients with Malignant Hyperthermia Susceptibility.

Patient name: example report **HN:** 123456789

METHODOLOGY

Genomic DNA is extracted from an individual at Bumrungrad Hospital. DNA sample is sent to the Macrogen, Korea to process Whole Exome Sequencing (WES). Library preparation, clustering and sequencing are processed on the Illumina platform to cover the coding regions of targeted genes ± ~10 bases of non-coding DNA flanking each exon. Raw data in an average at 6 Gb were generated. Reads from the sequence output were aligned to the human reference genome (GRCh37) using BWA. Variants are called using GATK pipeline. The tertiary analysis is performed at Bumrungrad Hospital. The variants were annotated and filtered using the Golden Helix VarSeq analysis workflow implementing the ACMG guidelines for the interpretation of sequence variants. This includes a comparison against the gnomAD population catalog of variants in 123,136 exomes, the 1000 Genomes Project Consortium's publication of 2,500 genomes, the NCBI ClinVar database of clinical assertions on variant's pathogenicity and multiple lines of computational evidence on conservation and functional impact.

Coverage Statistics for pharmacogenomics finding

Target region / Coverage	WES Target region	Pharmacogenomics finding target region
Mean depth (X)	**54.8X**	**53.7X**
Mean depth ≥ 10X	**95.1%**	**96.7%**

VARIANT ASSESSMENT PROCESS

The following databases and in-silico algorithms are used to annotate and evaluate the impact of the variant in the context of human disease: 1000 genomes, gnomAD, ClinVar, OMIM, dbSNP, NCIB RefSeq Genes, ExAC Gene Constraints, VS-SIFT, VS-PolyPhen2, PhyloP, GERP++, GeneSplicer, MaxEntScan, NNSplice, PWM Splice Predictor. Analysis was reported using the to HGVS nomenclature (www.hgvs.org/mutnomen) as implemented by the VarSeq transcript annotation algorithm. The reported transcript matches that used most frequently by the clinical labs submitting to ClinVar.

LIMITATIONS

It should be noted that the test result is limited to a set of genes indicated in the panel and might not cover all possible variants related to the particular condition. For some target regions, the depth covered for analysis may be variable. However, any targeted gene that fails to meet the acceptance criteria (Mean depth ≥ 10X) will be noted. Due to these limitations, ruling out the diagnosis of a genetic disorder should not be made based on negative results. An evaluation by alternative methods should be considered if a specific clinical disorder is suspected. This report only includes variants that meet a level of evidence threshold for cause or contribute to disease/condition. Reported variants are not confirmed by Sanger sequencing. Certain classes of genomic variants are also not covered using the NGS testing technology, including repeat expansions, large deletion or large duplication (≥50 kb), translocations and gene fusions or other complex structural rearrangements.

Patient name: example report **HN:** 123456789

DISCLAIMER

The result interpretation is based on the most current scientific and analytical standards ·However, more evidence for disease association of genes and causal pathogenic variants are discovered every year, and it is recommended that genetic variants are re-interpreted with updated software and annotations periodically ·There is also a possibility of an error in the result due to contaminants in the sample, rare technical errors, a rare genetic variant that could interfere with the analysis ·This test should be used in compliance with the other diagnostic test ·Note that this test cannot exclude the possibility of variants in genes not analyzed or assayed with incomplete coverage ·Even though this test is not designed to distinguish between somatic and germline variants, if variant of somatic is detected, supplementary testing may be compulsory to clarify the significance of results ·Genetic counseling is recommended to help understand the test result and explain the implications of this result for the patients and other family members. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary.

CONDITION ASSOCIATED GENE

The table shows the list of 2 genes related to pharmacogenomics panel analyzed in this test. Gene-Phenotype relationship information is retrieved from http:/www.omim.org

Gene	Transcript	Gene MIM number	Gene associated condition
CACNA1S	NM_000069.3	114208	Malignant hyperthermia
RYR1	NM_000540.3	180901	Malignant hyperthermia

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