INVITAE

INVITAE DIAGNOSTIC TESTING RESULTS

Patient name:		**Sample type:**	Buccal Swab	**Report date:**	13-NOV-2023
DOB:		**Sample collection date:**		**Invitae #:**	
Sex assigned at birth:	Male	**Sample accession date:**		**Clinical team:**	
Gender:					
Patient ID (MRN):					

Reason for testing

Diagnostic test for a personal history of disease

Test performed

Sequence analysis and deletion/duplication testing of the 241 genes listed in the Genes Analyzed section.

- Invitae Neurodevelopmental Disorders (NDD) Panel

RESULT: UNCERTAIN

Variant(s) of Uncertain Significance identified.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
DYNC1H1	c.9589C>G (p.Gln3197Glu)	heterozygous	Uncertain Significance
KMT2B	c.241C>T (p.Arg81Cys)	heterozygous	Uncertain Significance
RAI1	c.4288A>G (p.Thr1430Ala)	heterozygous	Uncertain Significance

About this test

This diagnostic test evaluates 241 gene(s) for variants (genetic changes) that are associated with genetic disorders. Diagnostic genetic testing, when combined with family history and other medical results, may provide information to clarify individual risk, support a clinical diagnosis, and assist with the development of a personalized treatment and management strategy.

Clinical comments

- When a single Variant of Uncertain Significance is found in a requisitioned gene that is only associated with autosomal recessive condition(s), it may not be included in the report.

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Next steps

- This test did NOT identify any pathogenic variants, but includes at least one result that is not completely understood at this time. Please note that the classification of variants may change over time as a result of new variant interpretation guidelines and/or new information. If an uncertain variant is reclassified, Invitae will update this report with the new interpretation and provide notification. This result should be discussed with a healthcare provider, such as a genetic counselor, to learn more about this result and the appropriate next steps for further evaluation. Clinical follow up may still be warranted. This result should be interpreted within the context of additional laboratory results, family history and clinical findings.

- Testing of up to two family members for the Variant(s) of Uncertain Significance (VUS) identified in DYNC1H1 and RAI1 is available at no additional cost. Please consider this individual's clinical features and availability of informative family members to test before ordering VUS resolution testing. More details on our VUS Resolution Program, including required documentation, can be found at **www.invitae.com/family**.

- Register your test at **www.invitae.com/patients** to download a digital copy of your results. You can also access educational resources about how your results can help inform your health.

Clinical summary

A Variant of Uncertain Significance, c.9589C>G (p.Gln3197Glu), was identified in DYNC1H1.

- The DYNC1H1 gene is associated with autosomal dominant Charcot-Marie-Tooth disease type 2O (CMT2O) (MedGen UID: 481850), lower extremity predominant spinal muscular atrophy 1 (SMALED1) (MedGen UID: 322470), and complex cortical dysplasia with brain malformations (MedGen UID: 482832).
- Not all variants present in a gene cause disease. The clinical significance of the variant(s) identified in this gene is uncertain. Until this uncertainty can be resolved, caution should be exercised before using this result to inform clinical management decisions.
- This variant qualifies for complimentary family studies as part of our VUS Resolution Program. Familial VUS testing is recommended if informative family members are available and are likely to provide additional evidence for future variant reclassification. Details on our VUS Resolution Program can be found at https://www.invitae.com/family.

A Variant of Uncertain Significance, c.241C>T (p.Arg81Cys), was identified in KMT2B.

- The KMT2B gene is associated with autosomal dominant childhood-onset dystonia (DYT28) (MedGen UID: 934600). Additionally, the KMT2B gene has preliminary evidence supporting a correlation with intellectual disability (PMID: 25405613).
- Not all variants present in a gene cause disease. The clinical significance of the variant(s) identified in this gene is uncertain. Until this uncertainty can be resolved, caution should be exercised before using this result to inform clinical management decisions.
- Complimentary familial VUS testing is not offered. Details on our VUS Resolution and Family Variant Testing Programs can be found at https://www.invitae.com/family.

A Variant of Uncertain Significance, c.4288A>G (p.Thr1430Ala), was identified in RAI1.

- The RAI1 gene is associated with autosomal dominant Smith-Magenis syndrome (MedGen UID: 162881), which usually results from a common 17p11.2 microdeletion that includes RAI1, as well as autosomal dominant Potocki-Lupski syndrome (PTLS) (MedGen UID: 894862), which usually results from a common 17p11.2 duplication that includes RAI1. Additionally, the RAI1 gene has preliminary evidence supporting a correlation with autosomal recessive non-syndromic deafness (PMID: 27082237).
- Not all variants present in a gene cause disease. The clinical significance of the variant(s) identified in this gene is uncertain. Until this uncertainty can be resolved, caution should be exercised before using this result to inform clinical management decisions.
- This variant qualifies for complimentary family studies as part of our VUS Resolution Program. Familial VUS testing is recommended if informative family members are available and are likely to provide additional evidence for future variant reclassification. Details on our VUS Resolution Program can be found at https://www.invitae.com/family.

Variant details

DYNC1H1, Exon 49, c.9589C>G (p.Gln3197Glu), heterozygous, Uncertain Significance

- This sequence change replaces glutamine, which is neutral and polar, with glutamic acid, which is acidic and polar, at codon 3197 of the DYNC1H1 protein (p.Gln3197Glu).
- This variant is not present in population databases (gnomAD no frequency).
- This variant has not been reported in the literature in individuals affected with DYNC1H1-related conditions.
- Advanced modeling of protein sequence and biophysical properties (such as structural, functional, and spatial information, amino acid conservation, physicochemical variation, residue mobility, and thermodynamic stability) performed at Invitae indicates that this missense variant is not expected to disrupt DYNC1H1 protein function with a negative predictive value of 95%.
- In summary, the available evidence is currently insufficient to determine the role of this variant in disease. Therefore, it has been classified as a Variant of Uncertain Significance.

KMT2B, Exon 1, c.241C>T (p.Arg81Cys), heterozygous, Uncertain Significance

- This sequence change replaces arginine, which is basic and polar, with cysteine, which is neutral and slightly polar, at codon 81 of the KMT2B protein (p.Arg81Cys).
- This variant is not present in population databases (gnomAD no frequency).
- This variant has not been reported in the literature in individuals affected with KMT2B-related conditions.
- Advanced modeling of protein sequence and biophysical properties (such as structural, functional, and spatial information, amino acid conservation, physicochemical variation, residue mobility, and thermodynamic stability) performed at Invitae indicates that this missense variant is not expected to disrupt KMT2B protein function with a negative predictive value of 80%.
- In summary, the available evidence is currently insufficient to determine the role of this variant in disease. Therefore, it has been classified as a Variant of Uncertain Significance.

RAI1, Exon 3, c.4288A>G (p.Thr1430Ala), heterozygous, Uncertain Significance

- This sequence change replaces threonine, which is neutral and polar, with alanine, which is neutral and non-polar, at codon 1430 of the RAI1 protein (p.Thr1430Ala).
- This variant is present in population databases (no rsID available, gnomAD 0.02%).
- This variant has not been reported in the literature in individuals affected with RAI1-related conditions.
- Advanced modeling of protein sequence and biophysical properties (such as structural, functional, and spatial information, amino acid conservation, physicochemical variation, residue mobility, and thermodynamic stability) performed at Invitae indicates that this missense variant is not expected to disrupt RAI1 protein function with a negative predictive value of 80%.
- In summary, the available evidence is currently insufficient to determine the role of this variant in disease. Therefore, it has been classified as a Variant of Uncertain Significance.

Genes analyzed

This table represents a complete list of genes analyzed for this individual, including the relevant gene transcript(s). If more than one transcript is listed for a single gene, variants were reported using the first transcript listed unless otherwise indicated in the report. An asterisk (*) indicates that this gene has a limitation. Please see the Limitations section for details. Results are negative unless otherwise indicated in the report. Benign and Likely Benign variants are not included in this report and in specific scenarios variants of uncertain significance in the requisitioned gene(s) may not be included in this report. These variants are available upon request.

GENE	TRANSCRIPT
ACTB	NM_001101.3
ACTG1	NM_001614.3
ADNP	NM_015339.4
ADSL	NM_000026.2
AGA	NM_000027.3
AHDC1	NM_001029882.3
ALDH5A1	NM_001080.3
ALDH7A1	NM_001182.4
AMER1	NM_152424.3
ANKRD11	NM_013275.5
AP1S2	NM_003916.4
ARG1	NM_000045.3
ARID1A	NM_006015.4
ARID1B	NM_020732.3
ARSA	NM_000487.5
ARX*	NM_139058.2
ASNS	NM_133436.3
ASXL1	NM_015338.5
ATP1A3	NM_152296.4
ATP7A	NM_000052.6
ATRX	NM_000489.4
AUTS2*	NM_015570.3
BCAP31	NM_001139441.1
BRAF	NM_004333.4
BRAT1	NM_152743.3
BRD4	NM_058243.2
BRWD3*	NM_153252.4
CACNA1A*	NM_001127221.1
CACNA1E	NM_000721.3
CAMK2B	NM_001220.4
CASK	NM_003688.3
CBL	NM_005188.3
CC2D2A	NM_001080522.2
CDK13*	NM_003718.4
CDKL5	NM_003159.2
CHD2	NM_001271.3
CHD7	NM_017780.3
CHD8	NM_001170629.1
CLCN4	NM_001830.3
CLN3	NM_001042432.1
CLN5	NM_006493.2
CLN6	NM_017882.2
CLTC	NM_001288653.1
CNTNAP2	NM_014141.5
COL4A1	NM_001845.5
CREBBP	NM_004380.2
CTNNB1	NM_001904.3
CUL3	NM_003590.4
DDC*	NM_000790.3
DDX3X*	NM_001193416.2
DEAF1	NM_021008.3
DHCR7	NM_001360.2
DNM1L	NM_012062.4
DNMT3A	NM_175629.2
DOCK6	NM_020812.3
DPF2	NM_006268.4
DYNC1H1	NM_001376.4
DYRK1A	NM_001396.3
EEF1A2	NM_001958.3
EFTUD2	NM_004247.3
EHMT1	NM_024757.4
EP300	NM_001429.3
EZH2*	NM_004456.4
FGD1	NM_004463.2
FOLR1	NM_016725.2
FOXG1	NM_005249.4
FOXP1	NM_032682.5
GABBR2	NM_005458.7
GABRB3	NM_000814.5
GABRG2	NM_000816.3
GALC*	NM_000153.3
GAMT	NM_000156.5
GATAD2B	NM_020699.3
GATM	NM_001482.2
GLB1	NM_000404.2
GM2A	NM_000405.4
GNAO1	NM_020988.2
GNAS*	NM_000516.5
GNS	NM_002076.3
GPC3*	NM_004484.3
GRIA3	NM_000828.4
GRIN1	NM_007327.3
GRIN2A	NM_000833.4
GRIN2B	NM_000834.3
HDAC8	NM_018486.2
HEXA	NM_000520.4
HEXB	NM_000521.3
HGSNAT	NM_152419.2
HIVEP2	NM_006734.3
HNRNPK	NM_002140.4
HNRNPU	NM_031844.2
HRAS	NM_005343.2
HUWE1	NM_031407.6
IDS*	NM_000202.6
IDUA	NM_000203.4
IGF1R	NM_000875.4
IL1RAPL1	NM_014271.3
IQSEC2	NM_001111125.2
ITPR1	NM_002222.5
KANSL1*	NM_001193466.1
KAT6A	NM_006766.4
KAT6B	NM_012330.3

GENE	TRANSCRIPT
KCNA2	NM_004974.3
KCNB1	NM_004975.2
KCNH1	NM_172362.2
KCNQ2	NM_172107.2
KCNT1	NM_020822.2
KDM5C	NM_004187.3
KDM6A*	NM_021140.3
KIF1A	NM_004321.6
KMT2A	NM_001197104.1
KMT2B	NM_014727.2
KMT2D	NM_003482.3
KMT2E*	NM_182931.2
KRAS	NM_004985.4
L1CAM	NM_000425.4
LZTR1	NM_006767.3
MAGEL2	NM_019066.4
MAN1B1	NM_016219.4
MAP2K1	NM_002755.3
MAP2K2	NM_030662.3
MBD5	NM_018328.4
MECP2	NM_004992.3;NM_001110792.1
MED12	NM_005120.2
MED13L	NM_015335.4
MEF2C	NM_002397.4
MFSD8	NM_152778.2
MID1*	NM_000381.3
MTOR	NM_004958.3
NAA10	NM_003491.3
NAA15	NM_057175.3
NAGLU	NM_000263.3
NALCN*	NM_052867.2
NEXMIF	NM_001008537.2
NF1*	NM_000267.3
NFIA*	NM_005595.4
NFIX	NM_001271043.2
NGLY1	NM_018297.3
NHS	NM_198270.3
NIPBL*	NM_133433.3
NONO	NM_001145408.1

GENE	TRANSCRIPT
NPC1	NM_000271.4
NR2F1	NM_005654.5
NRAS	NM_002524.4
NRXN1	NM_001135659.1
NSD1	NM_022455.4
NSUN2*	NM_017755.5
OCRL	NM_000276.3
OPHN1	NM_002547.2
OTC	NM_000531.5
PACS1*	NM_018026.3
PACS2	NM_001100913.2
PAH	NM_000277.1
PCBD1	NM_000281.3
PCDH19	NM_001184880.1
PDHA1	NM_000284.3
PGAP3	NM_033419.4
PHF21A	NM_001101802.1
PHF6	NM_032458.2
PHIP*	NM_017934.6
PLA2G6	NM_003560.2
PMM2	NM_000303.2
POLG	NM_002693.2
PPM1D	NM_003620.3
PPP1CB	NM_206876.1
PPP2R1A	NM_014225.5
PPP2R5D	NM_006245.3
PPP3CA	NM_000944.4
PPT1	NM_000310.3
PQBP1	NM_005710.2
PTEN*	NM_000314.4
PTPN11	NM_002834.3
PTS	NM_000317.2
PURA	NM_005859.4
QDPR	NM_000320.2
RAD21	NM_006265.2
RAF1	NM_002880.3
RAI1	NM_030665.3
RBM10	NM_005676.4
RIT1	NM_006912.5

GENE	TRANSCRIPT
RPS6KA3	NM_004586.2
SATB2	NM_015265.3
SCN1A	NM_001165963.1
SCN1B	NM_199037.3;NM_001037.4
SCN2A	NM_021007.2
SCN3A	NM_006922.3
SCN8A	NM_014191.3;NM_001330260.1
SETBP1	NM_015559.2
SETD5	NM_001080517.2
SGSH	NM_000199.3
SHOC2	NM_007373.3
SIN3A	NM_001145358.1
SLC13A5	NM_177550.4
SLC16A2	NM_006517.4
SLC2A1	NM_006516.2
SLC6A1	NM_003042.3
SLC6A8	NM_005629.3
SLC9A6*	NM_006359.2
SMARCA2*	NM_003070.4
SMARCA4	NM_001128849.1
SMARCB1	NM_003073.3
SMARCE1	NM_003079.4
SMC1A	NM_006306.3
SMC3	NM_005445.3
SON	NM_032195.2
SOS1	NM_005633.3
SOS2	NM_006939.2
SOX11	NM_003108.3
SPAST	NM_014946.3
SPATA5	NM_145207.2
SPTAN1	NM_001130438.2
STAG1	NM_005862.2
STXBP1	NM_003165.3
SURF1	NM_003172.3
SYNGAP1	NM_006772.2
TAF1	NM_004606.4
TBCK	NM_001163435.2
TBL1XR1	NM_024665.4
TCF20	NM_005650.3

GENE	TRANSCRIPT
TCF4	NM_001083962.1
TELO2	NM_016111.3
TPP1	NM_000391.3
TRAPPC9	NM_031466.7
TRRAP	NM_003496.3
TSC1*	NM_000368.4
TSC2	NM_000548.3
TUBA1A	NM_006009.3
UBE3A	NM_130838.1
UNC80	NM_032504.1
USP9X	NM_001039590.2
VPS13B	NM_017890.4
WDR45	NM_007075.3
WWOX	NM_016373.3
ZBTB18	NM_205768.2
ZBTB20	NM_001164342.2
ZC4H2	NM_018684.3
ZDHHC9	NM_016032.3
ZEB2	NM_014795.3
ZIC2	NM_007129.3
ZMIZ1	NM_020338.3
ZMYND11	NM_006624.5

Methods

- Genomic DNA obtained from the submitted sample is enriched for targeted regions using a hybridization-based protocol, and sequenced using Illumina technology. Unless otherwise indicated, all targeted regions are sequenced with ≥50x depth or are supplemented with additional analysis. Reads are aligned to a reference sequence (GRCh37), and sequence changes are identified and interpreted in the context of a single clinically relevant transcript, indicated in the Genes Analyzed table. Enrichment and analysis focus on the coding sequence of the indicated transcripts, 20bp of flanking intronic sequence, and other specific genomic regions demonstrated to be causative of disease at the time of assay design. Promoters, untranslated regions, and other non-coding regions are not otherwise interrogated. For some genes only targeted loci are analyzed. Exonic deletions and duplications are called using an in-house algorithm that determines copy number at each target by comparing the read depth for each target in the proband sequence with both mean read-depth and read-depth distribution, obtained from a set of clinical samples. Markers across the X and Y chromosomes are analyzed for quality control purposes and may detect deviations from the expected sex chromosome complement. Such deviations may be included in the report in accordance with internal guidelines. Variants are reported according to the Human Genome Variation Society (HGVS) guidelines. Confirmation of the presence and location of reportable variants is performed as needed based on stringent criteria using one of several validated orthogonal approaches (PubMed ID 30610921). Sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778). Confirmatory sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778). RNA sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778).

  The following additional analyses are performed if relevant to the requisition. For PMS2 exons 12-15, the reference genome has been modified to force all sequence reads derived from PMS2 and the PMS2CL pseudogene to align to PMS2, and variant calling algorithms are modified to support an expectation of 4 alleles. If a rare SNP or indel variant is identified by this method, both PMS2 and the PMS2CL pseudogene are amplified by long-range PCR and the location of the variant is determined by Pacific Biosciences (PacBio) SMRT sequencing of the relevant exon in both long-range amplicons. If a CNV is identified, MLPA or MLPA-seq is run to confirm the variant. If confirmed, both PMS2 and PMS2CL are amplified by long-range PCR, and the identity of the fixed differences between PMS2 and PMS2CL are sequenced by PacBio from the long-range amplicon to disambiguate the location of the CNV. For C9orf72 repeat expansion testing, hexanucleotide repeat units are detected by repeat-primed PCR (RP-PCR) with fluorescently labeled primers followed by capillary electrophoresis. Interpretation Reference Ranges: Benign (Normal Range): <25 repeat units, Uncertain: 25-30 repeat units, Pathogenic (Full Mutation): >=31 repeat units (PMID: 21944779, 22406228, 23111906, 28689190, 31315673, 33168078, 33575483). A second round of RP-PCR utilizing a non-overlapping set of primers is used to confirm the initial call in the case of suspected allele sizes of 22 or more repeats. For RNA analysis of the genes indicated in the Genes Analyzed table, complementary DNA is synthesized by reverse transcription from RNA derived from a blood specimen and enriched for specific gene sequences using capture hybridization. After high-throughput sequencing using Illumina technology, the output reads are aligned to a reference sequence (genome build GRCh37; custom derivative of the RefSeq transcriptome) to identify the locations of exon junctions through the detection of split reads. The relative usage of exon junctions in a test specimen is assessed quantitatively and compared to the usage seen in control specimens. Abnormal exon junction usage is evaluated as evidence in the Sherloc variant interpretation framework. If an abnormal splicing pattern is predicted based on a DNA variant outside the typical reportable range, as described above, the presence of the variant is confirmed by targeted DNA sequencing.

- A PMID is a unique identifier referring to a published, scientific paper. Search by PMID at **http://www.ncbi.nlm.nih.gov/pubmed**.
- An rsID is a unique identifier referring to a single genomic position, and is used to associate population frequency information with sequence changes at that position. Reported population frequencies are derived from a number of public sites that aggregate data from large-scale population sequencing projects, including ExAC (**http://exac.broadinstitute.org**), gnomAD (**http://gnomad.broadinstitute.org**), and dbSNP (**http://ncbi.nlm.nih.gov/SNP**).
- A MedGen ID is a unique identifier referring to an article in MedGen, NCBI's centralized database of information about genetic disorders and phenotypes. Search by MedGen ID at **http://www.ncbi.nlm.nih.gov/medgen**. An OMIM number is a unique identifier referring to a comprehensive entry in Online Mendelian Inheritance in Man (OMIM). Search by OMIM number at **http://omim.org/**.
- Invitae uses information from individuals undergoing testing to inform variant interpretation. If "Invitae" is cited as a reference in the variant details this may refer to the individual in this requisition and/or historical internal observations.

Limitations

Based on validation study results, this assay achieves >99% analytical sensitivity and specificity for single nucleotide variants, insertions and deletions <15bp in length, and exon-level deletions and duplications. Invitae's methods also detect insertions and deletions larger than 15bp but smaller than a full exon but sensitivity for these may be marginally reduced. Invitae's deletion/duplication analysis determines copy number at a single exon resolution at virtually all targeted exons. However, in rare situations, single-exon copy number events may not be analyzed due to inherent sequence properties or isolated reduction in data quality. Certain types of variants, such as structural rearrangements (e.g. inversions, gene conversion events, translocations, etc.) or variants embedded in sequence with complex architecture (e.g. short tandem repeats or segmental duplications), may not be detected. Additionally, it may not be possible to fully resolve certain details about variants, such as mosaicism, phasing, or mapping ambiguity. Unless explicitly guaranteed, sequence changes in the promoter, non-coding exons, and other non-coding regions are not covered by this assay. Please consult the test definition on our website for details regarding regions or types of variants that are covered or excluded for this test. This report reflects the analysis of an extracted genomic DNA sample. While this test is intended to reflect the analysis of extracted genomic DNA from a referred patient, in very rare cases the analyzed DNA may not represent that individual's constitutional genome, such as in the case of a circulating hematolymphoid neoplasm, bone marrow transplant, blood transfusion, chimerism, culture artifact or maternal cell contamination. Interpretations are made on the assumption that any clinical information provided, including specimen identity, is accurate. Invitae's RNA analysis is not designed for use as a stand-alone diagnostic method and cannot determine absolute RNA levels. Results from the RNA analysis may not be informative for interpreting copy number gains.

ARX: Analysis is validated to detect polyalanine expansions but sensitivity may be reduced. EZH2: Sequencing analysis for exons 20 includes only cds +/- 10 bp. GPC3: Sequencing analysis for exons 3 includes only cds +/- 10 bp. KANSL1: Deletion/duplication and sequencing analysis is not offered for exons 2-3. NF1: Sequencing analysis for exons 2, 7, 25, 41, 48 includes only cds +/- 10 bp. PTEN: Sequencing analysis for exons 8 includes only cds +/- 10 bp. SLC9A6: Sequencing analysis for exons 14 includes only cds +/- 10 bp. TSC1: Sequencing analysis for exons 21 includes only cds +/- 10 bp. GALC: Deletion/duplication analysis is not offered for exon 6. IDS: Detection of complex rearrangements not offered (PMID: 7633410, 20301451). KDM6A: Sequencing analysis for exons 18 includes only cds +/- 10 bp. NIPBL: Sequencing analysis is not offered for exon 33. CACNA1A: Trinucleotide repeat expansions are not determined on this assay. PACS1: Sequencing analysis is not offered for exon 1. NSUN2: Deletion/duplication analysis is not offered for exon 9. DDC: Deletion/duplication analysis is not offered for exons 10-11. CDK13: Sequencing analysis for exons 12 includes only cds +/- 10 bp. DDX3X: Sequencing analysis is not offered for exon 3. MID1: Sequencing analysis for exons 3 includes only cds +/- 0 bp. KMT2E: Sequencing analysis for exons 6 includes only cds +/- 10 bp. AUTS2: Sequencing analysis for exons 3 includes only cds +/- 10 bp. NALCN: Sequencing analysis for exons 19 includes only cds +/- 0 bp. GNAS: This test is not validated to detect or quantify variant mosaicism and caution should be used while interpreting results for this gene in which mosaicism or somatic variation is an established cause of disease. NFIA: Sequencing analysis for exons 9 includes only cds +/- 0 bp. BRWD3: Sequencing analysis for exons 9 includes only cds +/- 0 bp. SMARCA2: Deletion/duplication analysis is not offered for exons 4-5 and sequencing analysis is not offered for exon 4. PHIP: Deletion/duplication analysis is not offered for exons 3-4.

Disclaimer

DNA studies do not constitute a definitive test for the selected condition(s) in all individuals. It should be realized that there are possible sources of error. Errors can result from trace contamination, rare technical errors, rare genetic variants that interfere with analysis, recent scientific developments, and alternative classification systems. This test should be one of many aspects used by the healthcare provider to help with a diagnosis and treatment plan, but it is not a diagnosis itself. This test was developed and its performance characteristics determined by Invitae. It has not been cleared or approved by the FDA. The laboratory is regulated under the Clinical Laboratory Improvement Act (CLIA) as qualified to perform high-complexity clinical tests (CLIA ID: 05D2040778). This test is used for clinical purposes. It should not be regarded as investigational or for research.

This report has been reviewed and approved by:

Matteo Vatta, Ph.D., FACMG
Clinical Molecular Geneticist

INVITAE

VUS RESULTS GUIDE

What your results mean for you

No significant genetic changes ("pathogenic variants" or "mutations") were found in your genetic test. However, your test did find a genetic change called a variant of uncertain significance (VUS) in one or more of the genes tested. When we see a genetic change, but are unsure of its impact on health, it is called a variant of uncertain significance.

Right now, there is not enough information about the VUS to know whether it causes disease or not. A VUS is a common type of result. We all have many genetic changes that do not cause medical problems. Most of the time, we later learn that a VUS is not related to disease risk.

Your risk for disease could still be influenced by a combination of unidentified genetic, personal, lifestyle and/or environmental factors. So, it's important to talk to your healthcare provider if you have questions about your risk.

Create a plan with your healthcare provider

These genetic test results should be shared with your healthcare providers. The chance for you to develop a disease is not determined by genetic test results alone. Your provider can help you make informed decisions about your healthcare.

What your results mean for your family

Testing family members for a VUS is usually not recommended. However, your report will note if testing your family members will help us learn more about your specific VUS.

Although your genetic test did not find a significant genetic change, your family members have their own unique genetic makeup. Genetic testing can help them understand their overall chance of developing a genetic disease.

We (and others) are here to help

Genetic counseling can help you clearly and accurately understand your results so it's important to talk to your genetic counselor or other healthcare provider about your test results. Invitae also has board-certified genetic counselors who are available to answer questions about your test results or your personal or family medical history.

Log in to your patient portal (invitae.com) to view your results, search for a local or Invitae genetic counselor, or join Invitae's Patient Insight Network (PIN), a community where you can connect with other patients and share your experience.

This information in this results guide is meant to be used along with your genetic test results and other health information. It is not meant to replace a discussion with your healthcare provider and should not be considered or interpreted as medical advice.

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