Veritas
The Genome Company

myNewbornDNA Gene Panel Test

Name
DOB
Sex
Provider
Date of Report

Sample Type
Sample Collected
Sample Received
Batch ID
Customer ID

NEGATIVE RESULT: no clinically significant variant identified

ADDITIONAL FINDINGS

No additional variants of clinical significance were detected.

INTERPRETATION

Sequencing analysis of the 407 genes on the Veritas myNewbornDNA multi-gene panel test was performed and no pathogenic variants were detected. This reduces the likelihood but does not exclude the genetic conditions screened for by this test. Variants in other genes not screened for by this test or rarely undetected variants in the genes analyzed by this test may still be present.

Gene test results should be interpreted in the context of the child's clinical and family history. For patients with a personal or family history of a specific genetic disease, additional genetic testing may be indicated.

The diseases included on this test have a high likelihood of presenting with signs and symptoms in early childhood (typically before the age of 10 years. Children with these diseases may benefit significantly from early diagnosis and intervention. Medical management recommendations will depend on the gene in which the variant(s) was identified.

ADDITIONAL NOTES
Pathogenic and likely pathogenic variants in these 407 genes are associated with an increased risk for childhood onset genetic disease. The disease risk differs from gene to gene. For some of the genes on this panel, an exact disease risk may not currently be known. If a variant is detected in more than one gene, it may be difficult to assess the overall disease risk. Medical management recommendations will depend on the gene in which the variant(s) was identified.

Please talk to your physician to understand your child's risk for inherited childhood onset disease(s). Most accurate risk assessment requires comprehensive medical and family history evaluation, and we strongly recommend that all families undergoing genetic testing speak with a certified genetic counselor or other qualified medical professional. Any changes in screening or medical management based on these results should only be done through consultation with your child's physician. For patients with negative or inconclusive gene test results who are still considered at increased risk for disease based on their clinical or family histories, medical management and surveillance recommendations should be provided in accordance with established societal guidelines.

A DNA sample from one or both of the biological parents may be requested to help interpret the gene sequencing results of the child (proband). If parental samples are requested, then targeted testing will be utilized; these samples will not be studied for variants not previously identified in the proband. No independent interpretation of the parental results will be performed and as such, no separate reports will be issued.

METHODS AND LIMITATIONS

Veritas' myNewbornDNA test is a screening test for newborn babies and children, covering 407 genes that lead to diseases that are highly penetrant, typically of pediatric onset, or that meet Veritas' selection criteria. The test is performed on saliva, cord blood or whole blood. Extracted genomic DNA is processed by a capture-based assay and sequenced on a next-generation sequencer (Illumina). For sample tracking and quality assurance, each sample is also assessed with the Infinium QC Array-24 microarray (Illumina). Sequencing is performed in Veritas Genetics' CLIA licensed and CAP accredited laboratory. Sequencing data are aligned to the hg19 (build 37.1) human reference genome. Data analysis is performed with Veritas Genetics' custom bioinformatics pipeline, which uses both Bayesian and Heuristic-based statistical variant callers.

Regions with high sequence homology (as defined in PMID: 27228465) or other technical limitations of Next Generation Sequencing are not analyzed, see gene list for reference. Positions with less than 10X coverage are excluded from reporting unless confirmed by an alternate technology.

Analytic sensitivity is 99.9%, 95% CI [99.7%, 100%] for SNVs and 93.6%, 95% CI [88.2%, 97.0%] for small insertions/deletions. Analytical positive predictive value is 99.1%, 95% CI [98.8%, 99.4%] for SNVs and 94.9%, 95% CI [89.8%, 97.9%] for small insertions/deletions. Only inherited (germline) variants are detected, and not somatic variants, mosaicism, or heteroplasmy.

Initial filtering of variants is based on population frequency, variant type, and variant classifications in ClinVar (Landrum et al., 2015) as well as HGMD (Human Gene Mutation Database, Stenson et al., 2017). Variant interpretation is restricted to the set of 407 genes of the panel. For these genes, any novel loss of function variants as well as variants with at least one ClinVar entry with a classification of likely pathogenic or pathogenic or an HGMD label of "DM" will be fully interpreted by Veritas using ACMG standards (Richards et al., 2015). The final classification may differ from ClinVar. Variants classified as pathogenic or likely pathogenic are reported. Benign variants, likely benign variants and variants of uncertain significance (VUS) are not reported.

All reported pathogenic and likely pathogenic variants are confirmed with Sanger sequencing. Carrier state for recessive disorders is not reported.

Certain types of variations are not analyzed, including but not limited to repeat expansions, inversions, deletions, duplications, translocations and large structural rearrangements. Therefore, for genetic diseases known to be associated with such variant types, a disease specific test providing coverage of all necessary variant types should be considered. Negative results do not exclude the possibility of an undetected pathogenic variant. False negatives or positives can occur for a variety of reasons including technical issues, human error, and limited available scientific and clinical knowledge on data interpretation.

References

Zook JM. et al. Extensive sequencing of seven human genomes to characterize benchmark reference materials. Sci Data 2016;3: 160025 doi: 10.1038/sdata.2016.25. PMID: 27271295

Mandelker D et al. Navigating highly homologous genes in a molecular diagnostic setting: a resource for clinical next-generation sequencing. Genet Med 2016;18:1282-1289. PMID: 27228465

Landrum MJ et al. ClinVar: public archive of interpretations of clinically relevant variants. Nuc Acids Res 2016;44(1):D862–D868.

METHODS AND LIMITATIONS

doi: 10.1093/nar/gkv1222. PMID 26582918

Richards S et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med 2015;17:405-424. PMID 25741868

Stenson PD et al. The Human Gene Mutation Database: towards a comprehensive repository of inherited mutation data for medical research, genetic diagnosis and next-generation sequencing studies. Hum Genet 2017;136:665-677. PMID: 28349240

GENES TESTED

ABCC8, ABCC9, ABCD1 (95.7%), ABCG5, ACADM, ACADVL, ACAT1, ACSF3, ACTG1, ADA, ADGRV1, ADK, AGA, AGL, AGXT, AIP, AIRE, AK2, AKR1D1, ALB, ALDH7A1, ALDOB, ALMS1, ALPL, ANK1, APC, APOB, AQP2, ARG1, ARMC4 (97.0%), ARSA, ARSB, ASL, ASPA, ASS1, ATP6V1B1, ATP7A, ATP7B, AUH, AVPR2, BCHE, BCKDHA, BCKDHB, BLM, BMPR1A, BSND, BTD, C21ORF59, CACNA1C, CACNA1S, CALM1, CALM2, CARD11, CASQ2, CASR, CBS, CCDC114, CCDC151, CCDC39, CCDC40, CCDC65, CCNO, CD3D, CD3E, CD40LG, CDC73, CDH23, CFTR, CIB2, CLDN14, CLRN1, CNGA3, CNGB3, COL11A1, COL1A1, COL1A2, COL2A1, COL3A1, COL4A3, COL4A4, COL4A5, COL9A1, CORO1A (92.1%), CPS1, CPT1A, CPT2, CTNS, CYBA, CYBB, CYP11B1 (87.0%), CYP11B2 (87.0%), CYP1B1, CYP27A1, CYP27B1, DBT, DCLRE1C, DHCR7, DLD, DNAAF1, DNAAF5 (95.8%), DNAH11, DNAH5, DNAI1, DNAJB13, DNMT3B, DOCK8, DRC1, DSP, DUOX2 (96.5%), DUOXA2, DYX1C1, EDN3, ELANE, ELN, ELP1, EPB42, ERCC6, ESRRB, ETFA, ETFB, ETFDH, ETHE1, EYA1 (93.3%), F10, F11, F13A1, F13B, F2, F5, F7, F8 (99.4%), F9, FAH, FANCA, FANCB, FANCC, FANCD2 (96.6%), FANCG, FANCI, FBN1, FBP1, FGF3, FGFR3, FKTN, FOLR1, G6PC, G6PD, GAA, GALE, GALK1, GALNS, GALT, GAMT, GAS8, GATA1, GATA2, GATM, GBA (70.3%), GBE1, GCDH, GCH1, GCK, GGCX, GH1, GIF, GIPC3, GJB2, GJB6, GLA, GLUD1, GP1BB, GP6, GP9, GPSM2, GRHPR, GSS, GYS2, HADH, HADHA, HADHB, HAX1, HBB, HEXA, HLCS, HMGCL, HMGCS2, HNF1A, HNF4A, HOGA1, HPD, HPS1, HPS3, HPS4, HSD11B2, HSD17B10, HSD3B2, HSD3B7, IDS (83.0%), IDUA, IGSF1, IL2RA, IL2RG, IL7R, ILDR1, INS, ITGA2B, ITGB3 (96.3%), ITK, IVD, IYD, JAG1, JAK3, KCNH2, KCNJ10, KCNJ11, KCNJ5, KCNQ1, KCNQ2, KCNQ4 (85.9%), LAMA2, LAMP2, LDLR, LHX3, LIPA, LMBRD1, LOXHD1, LPL, LRPPRC, LRRC6, LRTOMT, MARVELD2, MAT1A, MAX, MCCC1, MCCC2, MCEE, MCIDAS, MCOLN1, MEFV, MEN1, MITF, MKS1, MLYCD, MMAA, MMAB, MMACHC, MMADHC, MPI, MPL, MTR, MTRR, MTTP, MUT, MYH9, MYO15A (98.2%), MYO6, MYO7A, NAGS, NDUFS6, NF1, NFKB2, NKX2-1, NKX2-6, NLRP3, NOTCH2 (95.4%), NPC1, NPC2, NPHS1, NPHS2, OAT, OTC, OTOA (65.4%), OTOF, OTOG, OTOGL, P2RY12, PAH, PAX3, PAX8, PCBD1, PCCA, PCCB, PCDH15, PDX1, PHGDH, PHKA2, PHKB, PHKG2, PIK3CD, PJVK, PKHD1, PLAU, PMM2, PNPO, POLR1D, POU1F1, POU3F4, PPT1, PROC, PROP1, PROS1 (92.6%), PRRT2, PTEN, PTPN11, PTPRC, PTPRQ, PTS, PYGL, PYGM, QDPR, RAB23, RAG1, RAG2, RB1, RET, RIT1, RMRP, RPL11, RPL5, RPS19, RPS24, RPS26, RPS29, RSPH1, RSPH3, RSPH4A, RSPH9, RYR1 (98.8%), S1PR2, SACS, SCN2A, SCN5A, SCN8A, SCNN1A, SCNN1B, SDHB, SIX1, SLC12A3, SLC12A6, SLC17A5, SLC19A2, SLC19A3, SLC22A5, SLC25A13, SLC25A15, SLC25A20, SLC26A2, SLC26A4, SLC2A1, SLC2A9, SLC37A4, SLC39A4, SLC46A1, SLC4A1, SLC5A5, SLC7A7, SLITRK6, SMAD4, SMPD1, SMPX, SNAI2, SOX10, SPAG1, SPG11, SPR, SRY, STAR, STAT3, STK11, STRC (16.9%), TAT, TAZ, TBC1D24, TBX19, TCIRG1, TCN2, TCOF1, TECTA, TG, TGFB3, TH, THRA, TMC1, TMIE, TMPRSS3, TP53, TPO, TRHR, TRIOBP (56.8%), TRMU, TSC1, TSC2, TSFM, TSHB, TSHR, TTC25, TTPA, UGT1A1, UNC13D, USH1C, USH1G, USH2A, VHL, WHRN, WT1, ZAP70, ZMYND10

Note: The percentage in parenthesis indicates the coverage of the codifying region in genes that, due to technical reasons, cannot be fully analyzed.

AUTHORIZED SIGNATURES

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DISCLAIMER

This test was developed and its performance characteristics determined by Veritas Genetics. The analytical validation of this test meets CLIA and CAP requirements. The test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The Veritas Genetics laboratory is regulated under CLIA as qualified to perform high-complexity testing. If you have any questions regarding the design and technical performance of this test, please contact us by phone at 1-888-507-6619 or email at clinical@veritasgenetics.com. If you have any clinical questions or wish to speak with one of Veritas' genetic counselors, please contact us by email at genetic.counseling@veritasint.com or visit https://www.veritasint.com/en/contact for local contact details.