Newborn Screening Panel

Kit ID: KITSAMPLE

Report Description

It is estimated that around 3%-4% of newborns have a genetic condition. The Newborn Screening Panel is a multi-gene panel aimed at investigating hundreds of disorders or diseases transmitted from parents to children and, in most cases, manifest themselves from the very first months of life.
More than 1000 genes related to pathologies inherited in an autosomal dominant, autosomal recessive and X-linked manner are investigated in this panel. Some of the diseases studied in the Newborn Screening Panel are the following: achondrogenesis, Alport disease, Bardet-Biedl syndrome 1 and argininosuccinic aciduria, among others. The Test offers an overview of pathologies affecting various organs and systems; in fact, diseases related to areas of interest such as neurology and neuromuscular disorders, endocrinology, metabolism, immunopathology, pulmonology and haematology are included.
The clinical impact of the Newborn Screening Panel is well reflected in its potential: infants suffering from medical conditions that have a particular effect on the quality of life need a rapid and precise diagnosis. This provides a fundamental contribution to the diagnostic process and to the therapeutic plan.

This test analyzes mutations consisting of Single Nucleotide Polymorphisms (SNPs) and small insertions/deletions (INDELs). - 1045 genes analyzed - 100% genomic regions covered - Intragenic and intergenic regions analyzed - All variants reported

In our analysis, we found pathogenic or likely pathogenic variants related to:

- Proline dehydrogenase deficiency
- Schizophrenia 4
- Methylmalonyl-CoA epimerase deficiency
- Hereditary fructosuria

Variants analyzed

F5 2	PC 1	CFH 1	DBT 1	DSP 1	INS 1	NF2 1	TTN 1	ACY1 1
ALG9 1	APOB 1	CPS1 1	GLDC 1	ICOS 1	LDLR 1	MCEE 1	PAX8 1	PLEC 1
RORC 1	SOS1 1	ALDOB 1	CHST6 1	COQ8A 1	CRPPA 1	F13A1 1	FANCA 1	FANCC 1
GANAB 1	MCCC2 1	MED12 1	NLRP3 1	ODAD1 1	PRODH 1	SFTPB 1	SPTA1 1	COL5A2 1
KCNJ11 1	CYP27A1 1	FASTKD2 1	SELENON 1	TBC1D24 1	TMPRSS3 1			

Summary Table

Pathogenic/Likely pathogenic variant(s) detected.

Gene	Coordinates	Nucleotide Change	rsID	Clinvar class.	Zygosity	Disease
ALDOB	9: 104189856	NM_000035.4(ALDOB):c.448G>C	rs1800546	Pathogenic	HET	Hereditary fructosuria, Fructose intolerance
MCEE	2: 71351575	NM_032601.4(MCEE):c.139C>T	rs111033538	Pathogenic	HET	Methylmalonyl-CoA epimerase deficiency, Methylmalonic aciduria

Clinical Variants Found

ALDOB

PATHOGENIC RARE HGMD

9 104189856 C>G

rs1800546 - NM_000035.4(ALDOB):c.448G>C (p.Ala150Pro)

Phenotypes

Hereditary fructosuria, Fructose intolerance

ZYG HET
MAF 0.0018
ACMG Likely pathogenic
CLIN. SIG Pathogenic [★★]
HGMD Rankscore 0.41
HGMD Variant Class DM

ALDOB Description

Cross et al. (1988) reported the first identification of a molecular lesion in the ALDOB gene in hereditary fructose intolerance (HFI; 229600). A G-to-C transversion in exon 5 of the ALDOB gene created a new recognition site for the restriction enzyme AhaII and resulted in an ala149-to-pro (A149P) substitution within a region critical for substrate binding. Utilizing this novel restriction site and the polymerase chain reaction (PCR), Cross et al. (1988) showed that the patient was homozygous. Three other patients with hereditary fructose intolerance unrelated to the original patient were found to have the same mutation; 2 were homozygous and 1 was compound heterozygous with another mutation in the ALDOB gene.

PubMed 3383242

Cross and Cox (1989) used allele-specific oligonucleotide probes to detect the A149P mutation in other pedigrees. They found the same mutation in all 12 British patients examined. Diagnosis of both homozygotes and heterozygotes could be achieved by specific amplification of DNA derived from mouthwash samples followed by hybridization to allele-specific oligonucleotides.

PubMed 2623136

In a study of patients with fructose intolerance drawn widely from Europe and the U.S., Cross et al. (1990) found the A149P mutation in 67% of alleles tested. The mutation was significantly more common in patients from northern than from southern Europe.

PubMed 1967768

Brooks and Tolan (1993) studied the possible origin of the A149P mutation, which accounts for 57% of fructose intolerance chromosomes. In 15 homozygotes they found absolute linkage disequilibrium between the A149P mutation and a particular 2-site RFLP, suggesting a single origin and founder effect.

PubMed 8096362

Dursun et al. (2001) screened 13 Turkish patients with hereditary fructose intolerance for 3 common mutations. Nine of the patients were homozygous for the A149P mutation, which corresponded to a frequency of about 55%.

PubMed 11757579

Davit-Spraul et al. (2008) identified the A149P mutation, which they referred to as ALA150PRO (A150P), in 64% of mutant alleles from 162 patients from 92 families with hereditary fructose intolerance. Most of the patients were French.

PubMed 18541450

MCEE

PATHOGENIC RARE HGMD

2 71351575 G>A

rs111033538 - NM_032601.4(MCEE):c.139C>T (p.Arg47Ter)

Phenotypes

Methylmalonyl-CoA epimerase deficiency, Methylmalonic aciduria

ZYG HET
MAF 0.00025
ACMG Pathogenic
CLIN. SIG Pathogenic [★★]
HGMD Rankscore 0.99
HGMD Variant Class DM

MCEE Description

Bikker et al. (2006) described a female patient born to consanguineous Caucasian parents with methylmalonyl-CoA epimerase deficiency (251120) and dystonia due to sepiapterin reductase deficiency (612716). The methylmalonyl-CoA epimerase deficiency was found to be caused by homozygosity for a 139C-T transition in exon 2 of the MCEE gene that resulted in an arg47 to ter substitution (R47X). This nonsense mutation was

predicted to result in an inactive epimerase enzyme, since the transcript would probably be rapidly degraded by nonsense-mediated decay; alternatively, if the transcript were stable, only a small part of it would be translated, because of the early termination signal. The patient was homozygous for a second mutation, in the SPR gene resulting in sepiapterin reductase deficiency (182125.0005); both parents were heterozygous for both mutations. Both genes map to chromosome 2. However, the sepiapterin reductase mutation in this family was a missense mutation, thus excluding the possibility of a contiguous gene syndrome. The clinical presentation of this patient closely resembled that described in a case of sepiapterin reductase deficiency with dystonia as the most prominent symptom. Bikker et al. (2006) suggested that since this patient was homozygous for 2 mutations, it was likely that methylmalonyl-CoA epimerase deficiency does not have a large clinical impact, or could even be considered as a nondisease.

PubMed 16752391

Dobson et al. (2006) reported a patient previously identified as belonging to the cobalamin A (cblA) complementation group (251100) but lacking mutations in the affected gene MMAA (607481). The patient's fibroblasts had normal levels of adenosylcobalamin compared to controls, whereas other cblA cell lines typically had reduced levels of the cofactor. The patient also had a milder form of methylmalonic aciduria than usually observed in cblA patients. The patient was homozygous for the R47X mutation in MCEE. One sib, also with mild methylmalonic aciduria, was also homozygous for the mutation. Both parents and one other sib were heterozygous. To assess the impact of isolated MCEE deficiency in cultured cells, HeLa cells were transfected with siRNA against MCEE. The reduced level of MCEE mRNA resulted in reduction of [(14)C]-propionate incorporation into cellular macromolecules. However, siRNA led to only a small reduction in pathway activity, suggesting that previously postulated nonenzymatic conversion of D- to L-methylmalonyl-CoA may contribute to some flux through the pathway.

PubMed 16697227

PRODH

HGMD

22 18905964 C>T

rs2904552 - NM_016335.6(PRODH):c.1292G>A (p.Arg431His)

ZYG HET
MAF 0.04293
ACMG Benign
CLIN. SIG Likely pathogenic [★]
HGMD Rankscore 0.1
HGMD Variant Class DFP

Phenotypes

Proline dehydrogenase deficiency, Schizophrenia 4, Hyperprolinaemia

PRODH Description

For discussion of the arg431-to-his (R431H) mutation in the PRODH gene that was found in compound heterozygous state in a patient with schizophrenia-4 (SCZD4; 600850) and hyperprolinemia (HYRPRO1; 239500) by Jacquet et al. (2002), see 606810.0004.

PubMed 12217952

Bender et al. (2005) found that the R431H mutation was associated with a moderate reduction in PRODH activity (30 to 70%).

PubMed 15662599

APOB

CONFLICTING HGMD

2 21231592 G>A

rs6413458 - NM_000384.3(APOB):c.8148C>T (p.Ile2716=)

ZYG HET
MAF 0.01438
ACMG Benign
CLIN. SIG Conflicting interpretations of pathogenicity [★]
HGMD Variant Class DM?

Phenotypes

Familial hypercholesterolemia, Familial hypercholesterolemia 1, Familial hypercholesterolemia 2, Hypobetalipoproteinemia, familial, 1, Hypercholesterolaemia

CFH

CONFLICTING RARE HGMD

1 196716375 C>T

rs121913059 - NM_000186.4(CFH):c.3628C>T (p.Arg1210Cys)

ZYG HET

MAF 0.00017

ACMG Likely pathogenic

CLIN. SIG Conflicting interpretations of pathogenicity [★]

HGMD Rankscore 0.23

HGMD Variant Class DM

Phenotypes

Basal laminar drusen, Atypical hemolytic-uremic syndrome 1, Factor H deficiency, Age-related macular degeneration 4, Atypical hemolytic uremic syndrome, CFH-Related Dense Deposit Disease / Membranoproliferative Glomerulonephritis Type II, Factor H deficiency

CFH Description

Complement Component H Deficiency

In a patient with complement factor H deficiency (CFHD; 609814), Servais et al. (2007) identified a heterozygous mutation in the CFH gene, resulting in an arg1210-to-cys (R1210C) substitution in the SCR20 region. The patient developed glomerulonephritis with isolated C3 deposits.

PubMed 17018561

Atypical Hemolytic Uremic Syndrome 1, Susceptibility To

Manuelian et al. (2003) reported a patient with atypical hemolytic uremic syndrome (AHUS1; 235400) in whom they identified a heterozygous 3701C-T transition in the CFH gene, resulting in the R1210C substitution. In vitro functional expression studies showed that the mutant protein had decreased binding to heparin, C3b/C3d, and human endothelial cells.

PubMed 12697737

Age-Related Macular Degeneration 4, Susceptibility To

Raychaudhuri et al. (2011) phased genotypes for 20 common SNPs spanning the CFH-CFHR1-CFHR3 region and a common CFHR1-CFHR3 deletion in 711 individuals with advanced age-related macular degeneration (see ARMD4; 610698) and 1,041 controls, and identified a rare high-risk haplotype ('H5') that lacked both the Y402H (134370.0008) and rs10737680-rs1410996 (134370.0016) risk alleles, but contained the R1210C substitution. Genotyping R1210C in 2,423 ARMD cases and 1,122 controls demonstrated high penetrance (present in 40 cases vs 1 control; p = 7.0 x 10(-6)) and an association with a 6-year-earlier onset of disease (p = 2.3 x 10(-6)). Because R1210C is known to cause familial renal disease, Raychaudhuri et al. (2011) assessed renal function in 17 unrelated R1210C heterozygotes with advanced ARMD but found no evidence of clinically significant renal dysfunction; in addition, comparing renal function in the R1210C heterozygotes to that of 17 ARMD patients matched for disease severity, age, and gender, but without R1210C, there was no significant difference.

PubMed 22019782

Zhan et al. (2013) sequenced 2,335 ARMD cases and 789 controls in 10 candidate loci (57 genes) and then augmented their control set with ancestry-matched exome-sequenced controls. An analysis of coding variation in 2,268 ARMD cases and 2,268 ancestry-matched controls identified 2 large-effect rare variants: R1210C in the CFH gene, with a case frequency of 0.51%, control frequency of 0.02%, and odds ratio of 23.11; and K155Q in the C3 gene (120700.0010), with a case frequency of 1.06%, control frequency of 0.39%, and odds ratio of 2.68. The variants suggested decreased inhibition of C3 by CFH, resulting in increased activation of the alternative complement pathway, as a key component of disease biology.

PubMed 24036949

Ferrara and Seddon (2015) analyzed images from a total of 143 ARMD patients (283 eyes), including 62 patients with the R1210C variant. Patients with the R1210C variant compared to those without this variant had the highest level of macular and total macular drusen scores (57.9% vs 16.7% and 52.0% vs 14.2%, respectively; p less than .001 for both scores) as well as a greater likelihood of having advanced disease (odds ratio, 7.0; 95% CI, 3.1-16.2; p less than .001). A higher prevalence of geographic atrophy was observed among patients carrying the R1210C variant (odds ratio, 13.7%; 95% CI, 5.0-37.7; p less than .001).

PubMed 25880396

COL5A2 CONFLICTING RARE

2 189907963 C>T

rs199802059 - NM_000393.5(COL5A2):c.3385G>A (p.Asp1129Asn)

Phenotypes

Connective tissue disease, Ehlers-Danlos syndrome, classic type

ZYG HET

MAF 0.00008

ACMG Uncertain significance

CLIN. SIG Conflicting interpretations of pathogenicity [★]

COQ8A CONFLICTING RARE

1 227152814 C>T

rs111529228 - NM_020247.5(COQ8A):c.291C>T (p.Ser97=)

Phenotypes

Coenzyme Q10 deficiency, primary, 4, Autosomal recessive cerebellar ataxia

ZYG HET

MAF 0.0016

ACMG Likely benign

CLIN. SIG Conflicting interpretations of pathogenicity [★]

CPS1 CONFLICTING RARE

2 211442212 G>A

rs114819130 - NM_001875.5(CPS1):c.449G>A (p.Gly150Glu)

Phenotypes

Carbamoyl-phosphate synthase I deficiency, Congenital hyperammonemia, type I

ZYG HET

MAF 0.002

ACMG Uncertain significance

CLIN. SIG Conflicting interpretations of pathogenicity [★]

CYP27A1 CONFLICTING RARE HGMD

2 219678877 C>T

rs41272687 - NM_000784.4(CYP27A1):c.1151C>T (p.Pro384Leu)

Phenotypes

Cholestanol storage disease, Cerebrotendinous xanthomatosis

ZYG HET

MAF 0.00859

ACMG Uncertain significance

CLIN. SIG Conflicting interpretations of pathogenicity [★]

HGMD Rankscore 0.13

HGMD Variant Class DM?

DSP

CONFLICTING RARE

6 7584173 T>A

rs149070106 - NM_004415.4(DSP):c.6678T>A (p.Gly2226=)

Phenotypes

Cardiomyopathy, Dilated cardiomyopathy with woolly hair and keratoderma, Arrhythmogenic right ventricular dysplasia 8, Skin fragility-woolly hair-palmoplantar keratoderma syndrome, Lethal acantholytic epidermolysis bullosa, Cardiovascular phenotype

ZYG HET

MAF 0.0004

ACMG Benign

CLIN. SIG Conflicting interpretations of pathogenicity [★]

F5

CONFLICTING HGMD

1 169521849 T>C

rs6035 - NM_000130.5(F5):c.1242A>G (p.Lys414=)

Phenotypes

Thrombophilia due to factor V Leiden, Thrombosis: increased risk

ZYG HET

MAF 0.08307

ACMG Benign

CLIN. SIG Conflicting interpretations of pathogenicity [★]

HGMD Variant Class R

FANCA

CONFLICTING RARE

16 89865630 G>A

rs752311383 - NM_000135.4(FANCA):c.837C>T (p.Asp279=)

Phenotypes

Fanconi anemia, complementation group A, Fanconi anemia

ZYG HET

MAF 0.00002

ACMG Likely benign

CLIN. SIG Conflicting interpretations of pathogenicity [★]

GANAB

CONFLICTING

11 62400108 G>A

rs1063445 - NM_198334.3(GANAB):c.925C>T (p.Arg309Cys)

Phenotype

Chronic kidney disease

ZYG HET

MAF 0.01038

ACMG Benign

CLIN. SIG Conflicting interpretations of pathogenicity [★]

GLDC CONFLICTING

9 6645310 C>A

rs141601131 - NM_000170.3(GLDC):c.190G>T (p.Ala64Ser)

Phenotype

Non-ketotic hyperglycinemia

ZYG HET

MAF -

ACMG Uncertain significance

CLIN. SIG Conflicting interpretations of pathogenicity [★]

INS CONFLICTING RARE

11 2181080 G>A

rs200306755 - NM_000207.3(INS):c.*2C>T

Phenotypes

Maturity-onset diabetes of the young, type 10, Transient Neonatal Diabetes, Dominant/Recessive

ZYG HET

MAF 0.00013

ACMG -

CLIN. SIG Conflicting interpretations of pathogenicity [★]

KCNJ11 CONFLICTING RARE

11 17408496 C>T

rs8175351 - NM_000525.4(KCNJ11):c.1143G>A (p.Lys381=)

Phenotypes

Islet cell hyperplasia, Transient neonatal diabetes mellitus 3, Maturity-onset diabetes of the young, type 13, Permanent neonatal diabetes mellitus

ZYG HET

MAF 0.00439

ACMG Likely benign

CLIN. SIG Conflicting interpretations of pathogenicity [★]

LDLR CONFLICTING

19 11221454 T>C

NM_000527.5(LDLR):c.1060+7=

Phenotype

Familial hypercholesterolemia 1

ZYG HOM

MAF -

ACMG -

CLIN. SIG Conflicting interpretations of pathogenicity [★]

MED12 CONFLICTING RARE

X 70342211 T>C

rs187377817 - NM_005120.3(MED12):c.1248+15T>C

ZYG HOM

MAF 0.00079

ACMG -

CLIN. SIG Conflicting interpretations of pathogenicity [★]

NLRP3 CONFLICTING HGMD

1 247588858 C>A

rs35829419 - NM_001243133.2(NLRP3):c.2107C>A (p.Gln703Lys)

Phenotypes

Familial cold autoinflammatory syndrome 1, Familial amyloid nephropathy with urticaria AND deafness, Chronic infantile neurological, cutaneous and articular syndrome, Cryopyrin associated periodic syndrome, Cryopyrin-associated periodic syndrome: atypical

ZYG HET

MAF 0.02236

ACMG Benign

CLIN. SIG Conflicting interpretations of pathogenicity [★]

HGMD Rankscore 0.1

HGMD Variant Class DM?

PC CONFLICTING RARE

11 66638540 C>A

rs147945506 - NM_001040716.2(PC):c.616G>T (p.Val206Leu)

Phenotype

Pyruvate carboxylase deficiency

ZYG HET

MAF 0.00399

ACMG Likely benign

CLIN. SIG Conflicting interpretations of pathogenicity [★]

PLEC CONFLICTING RARE

8 144999499 C>T

rs201430180 - NM_201384.3(PLEC):c.4598G>A (p.Arg1533Gln)

Phenotypes

Epidermolysis bullosa simplex, Ogna type, Epidermolysis bullosa simplex with muscular dystrophy, Epidermolysis bullosa simplex with pyloric atresia, Limb-girdle muscular dystrophy, type 2Q, Epidermolysis bullosa simplex with nail dystrophy

ZYG HET

MAF 0.0024

ACMG Likely benign

CLIN. SIG Conflicting interpretations of pathogenicity [★]

SELENON CONFLICTING

1 26126680 T>C

rs12121707 - NM_020451.2(SELENON):c.-42T>C

Phenotype

SEPN1-Related Disorders

ZYG HOM

MAF -

ACMG -

CLIN. SIG Conflicting interpretations of pathogenicity [★]

SPTA1 CONFLICTING RARE HGMD

1 158612719 C>T

rs41273523 - NM_003126.4(SPTA1):c.4490G>A (p.Gly1497Glu)

Phenotypes

Hereditary pyropoikilocytosis, Elliptocytosis 2, Spherocytosis type 3, Spherocytosis

ZYG HET

MAF 0.00639

ACMG Benign

CLIN. SIG Conflicting interpretations of pathogenicity [★]

HGMD Rankscore 0.13

HGMD Variant Class DM

ACY1

3 52020311 C>T

NM_000666.3(ACY1):c.400C>T (p.Arg134Trp)

ZYG HET

MAF -

ACMG Uncertain significance

CLIN. SIG Uncertain significance [★]

ALG9

11 111654648 T>A

rs2554994 - NM_024740.2(ALG9):c.*2473A>T

Phenotype

ALG9 congenital disorder of glycosylation

ZYG HOM

MAF -

ACMG -

CLIN. SIG Uncertain significance [★]

CHST6

16 75508248 A>G

NM_021615.5(CHST6):c.*4291T>C

Phenotype

Macular corneal dystrophy

ZYG HET
MAF -
ACMG -
CLIN. SIG Uncertain significance [★]

CRPPA

7 16128940 C>T

rs28444529 - NM_001101426.4(CRPPA):c.*2380G>A

Phenotypes

Congenital Muscular Dystrophy, alpha-dystroglycan related

ZYG HET
MAF 0.33247
ACMG -
CLIN. SIG Uncertain significance [★]

DBT

1 100654909 A>T

NM_001918.5(DBT):c.*6902T>A

Phenotype

Maple syrup urine disease

ZYG HOM
MAF -
ACMG -
CLIN. SIG Uncertain significance [★]

F13A1

6 6144807 G>C

NM_000129.4(F13A1):c.*1045C>G

Phenotypes

Factor XIII, A subunit, deficiency of

ZYG HET
MAF -
ACMG -
CLIN. SIG Uncertain significance [★]

FANCC

9 98009494 C>T

NM_000136.3(FANCC):c.250+220G>A

ZYG HET
MAF -
ACMG -
CLIN. SIG Uncertain significance

FASTKD2

2 207660256 C>T

NM_001136193.2(FASTKD2):c.*3730C>T

Phenotype

Mitochondrial complex IV deficiency

ZYG HET
MAF -
ACMG -
CLIN. SIG Uncertain significance [★]

ICOS

2 204825615 T>C

rs528769953 - NM_012092.4(ICOS):c.*1293T>C

Phenotype

Common variable immunodeficiency 1

ZYG HET
MAF -
ACMG -
CLIN. SIG Uncertain significance [★]

MCCC2

5 70953930 G>C

NM_022132.5(MCCC2):c.*1243G>C

Phenotype

3-methylcrotonyl CoA carboxylase 2 deficiency

ZYG HET
MAF -
ACMG -
CLIN. SIG Uncertain significance [★]

NF2

22 30092078 T>C

NM_000268.4(NF2):c.*1287T>C

Phenotypes

Neurofibromatosis, type 2

ZYG HET
MAF -
ACMG -
CLIN. SIG Uncertain significance [★]

ODAD1

19 48821738 C>T

NM_001364171.2(ODAD1):c.266G>A (p.Arg89Gln)

Phenotype

Primary ciliary dyskinesia

ZYG HET
MAF -
ACMG Uncertain significance
CLIN. SIG Uncertain significance [★]

PAX8 RARE

2 113984717 C>T

rs149585280 - NM_003466.4(PAX8):c.1189+15G>A

Phenotypes

Hypothyroidism, congenital, nongoitrous, 2

ZYG HET
MAF 0.0024
ACMG -
CLIN. SIG Uncertain significance [★]

RORC RARE

1 151789185 G>A

rs142141845 - NM_005060.4(RORC):c.253C>T (p.His85Tyr)

Phenotype

Immunodeficiency 42

ZYG HET
MAF 0.0004
ACMG Uncertain significance
CLIN. SIG Uncertain significance [★]

SFTPB RARE

2 85895365 C>T

rs762253717 - NM_000542.3(SFTPB):c.-23G>A

Phenotypes

Surfactant metabolism dysfunction, pulmonary, 1

ZYG HET
MAF 0.00032
ACMG -
CLIN. SIG Uncertain significance [★]

SOS1 RARE HGMD

2 39278394 A>G

rs142094234 - NM_005633.4(SOS1):c.755T>C (p.Ile252Thr)

Phenotype

Noonan syndrome

ZYG HET

MAF 0.0002

ACMG Uncertain significance

CLIN. SIG Uncertain significance [★]

HGMD Rankscore 0.92

HGMD Variant Class DM

TBC1D24 RARE

16 2546588 G>A

rs267607103 - NM_001199107.2(TBC1D24):c.439G>A (p.Asp147Asn)

Phenotypes

Epileptic encephalopathy, early infantile, 1, Myoclonic epilepsy, familial infantile, Deafness, autosomal dominant 65, Caused by mutation in the TBC1 domain family, member 24

ZYG HET

MAF 0.00014

ACMG Uncertain significance

CLIN. SIG Uncertain significance [★★]

TMPRSS3

21 43792066 A>G

NM_001256317.3(TMPRSS3):c.*805T>C

Phenotypes

Deafness, autosomal recessive 8

ZYG HET

MAF -

ACMG -

CLIN. SIG Uncertain significance [★]

TTN RARE HGMD

2 179590654 G>A

rs751534449 - NM_001267550.2(TTN):c.20395C>T (p.Arg6799Trp)

Phenotypes

Hypertrophic cardiomyopathy, Skeletal myopathy

ZYG HET

MAF 0.00003

ACMG Uncertain significance

CLIN. SIG Uncertain significance [★★]

HGMD Rankscore 0.27

HGMD Variant Class DM

Informational Variants Found

F5 HGMD

1 169519049 T>C

rs6025 - NM_000130.5(F5):c.1601= (p.Arg534=)

ZYG HOM

MAF -

ACMG Uncertain significance

CLIN. SIG Drug response [★★★]

HGMD Rankscore 0.32

HGMD Variant Class DFP

Phenotypes

Factor V deficiency, hormonal contraceptives for systemic use response - Toxicity/ADR, Thrombosis: increased risk

Related Conditions:

- Proline dehydrogenase deficiency
- Schizophrenia 4
- Methylmalonyl-CoA epimerase deficiency
- Hereditary fructosuria

Genes Analyzed

This report analyzed the following genes:

GNPTAB, MPI, ALG14, ACADVL, GNAS, CAVIN1, NDUFS1, CHKB, NKX2-1, LAMA2, BRAT1, CHRND, IFIH1, CLPB, CIITA, BOLA3, SUMF1, AARS1, F7, IGF1, LIPT2, STT3A, NDUFS4, SDHA, SOX9, UQCRC2, PDE10A, F8, FGA, EPCAM, RFT1, TECTA, KCTD7, CDK5RAP2, TSHB, GBE1, HAX1, TNFRSF13C, ALPL, GP1BA, FIG4, COL2A1, CD79A, DOCK7, NF2, SOS1, STK11, CORO1A, GCK, MRPL3, ALG2, ALDH6A1, B4GALT7, PAX8, POFUT1, HPS1, IFT172, TBX19, SLC7A9, AGK, HSD17B4, PKLR, RFX5, NPC2, UROS, SCN4A, CD81, CYP7B1, EDN3, CCDC103, KCNQ3, MVK, CEP152, PDHB, DHCR7, ETFA, CLCNKB, SLC33A1, SLC26A4, ALDH18A1, HBA2, TP63, NANS, PEX14, VDR, TNFSF4, XPC, TG, SPTA1, ITGB3, NF1, LIG4, COL7A1, DSE, MAN1B1, NEU1, RB1, ELAC2, SSR4, GDAP1, ARL6, HNF1A, GJA1, KRAS, NFU1, NIPAL4, XYLT2, PIGM, NDUFB3, POMGNT2, CHRNB1, DPM2, KCNQ2, CHST3, ZIC3, ACOX2, CXCR4, DPAGT1, MAP2K1, MTO1, NR0B1, RPE65, NAGS, CYP21A2, CNTN1, ALDH4A1, GFAP, CAST, MYO7A, ALG6, IL2RA, EGR2, AP4E1, LAS1L, SFTPC, MKKS, B4GAT1, USH1C, NOTCH2, PKHD1, LIPA, NEB, COPA, ALS2, DNAI2, HADHA, ABCB11, NEXN, FOXE1, PDHA1, B4GALT1, SLC25A15, DSP, B3GALT6, AP2S1, ADSL, HADHB, FKTN, SLC12A6, ABCD4, UBA1, GNS, POMT1, RAB3GAP1, HNF4A, NGLY1, PIGV, COG7, GLUD1, AP4M1, CYP17A1, PEX16, PIGY, BTK, MMACHC, NDUFV1, CLCNKA, ADAMTS13, DDR2, PLOD1, NDUFAF2, NDUFA11, ACADS, CACNA1C, RORC, CSGALNACT1, NDUFA1, APOB, GJB2, COG6, SLC2A1, OXCT1, TAFAZZIN, CHSY1, MPC1, CFHR3, GANAB, LRBA, NRAS, CHST14, PNPLA1, CCDC115, ADNP, CD3E, CFL2, COL11A1, NKX2-5, SERPINC1, SLC5A1, CR2, SLC22A5, MAGEL2, HEXB, SLCO1B3, GYS2, B4GALNT1, RAB3GAP2, TRIOBP, SMAD4, USH1G, CPT2, PAFAH1B1, ALG13, TBC1D24, COL1A2, TBX5, SLC25A12, MMAA, MLYCD, MTRFR, ENG, SHOC2, CYP27A1, DEPDC5, CLN6, GARS1, MFSD8, GPC3, CD19, ALAD, PPM1K, PRRT2, STIM1, EIF2B1, POR, ANKRD26, CRLF1, DNAH5, TRHR, CD3D, PYGL, CHD7, SIL1, CFTR, ALOXE3, DBT, PGM3, NCF1, TMEM165, PLCB4, COL5A2, OPHN1, ETFB, TRAPPC2, DOK7, GALC, ACO2, CYP4F22, SLC9A7, MOGS, NDUFAF3, KAT6B, DOCK8, F2, ALDOA, KCNJ10, PIGW, NDUFAF5, SDHAF1, STAR, IGSF1, IRF8, KIF1B, PNPO, ARSA, BCKDHB, GSS, CYP27B1, FKBP14, CDAN1, GCH1, KCNH1, GLDC, CAV1, CLDN16, TUSC3, KCNE1, MALT1, GPHN, DLD, CTSA, ADK, LDLR, GLRA1, STAT3, CD40, COL1A1, CTSD, FGB, IYD, PIK3CD, SPTB, NAGA, KRT5, NALCN, TRIP11, CAV3, CPS1, GRHPR, TSHR, SPTAN1, TPO, CASK, AGXT, COL17A1, CRTAP, PDCD10, ENPP1, RAPSN, AHCY, BRAF, SLC30A2, MTM1, KAT6A, EOGT, SNX10, TSC2, CASR, ALOX12B, ISCA2, MTR, EYA4, CLN8, SPEG, UMPS, NDUFB9, RANBP2, MPV17, SPRED1, ST3GAL5, CACNB2, COG1, COMP, THRA, NDUFS3, GLRB, EIF2B5, NDUFS6, ACAD9, ANKH, TCAP, CYBA, IL2RG, PAX3, BCKDK, ALDOB, SLC35A3, TTPA, BCKDHA, RAG2, SECISBP2, IER3IP1, PIGQ, LPIN1, CUL4B, DUOXA2, FKRP, TMPRSS3, HCFC1, SCN9A, ATP8B1, HADH, RET, TFR2, CLN5, ARCN1, CD79B, MPZ, GLIS3, DPM1, WHRN, CPT1A, CFH, LARS2, F13A1, COL6A2, COX15, POGZ, PROS1, SUCLA2, IBA57, MYH9, SIX3, HGSNAT, DNAJC12, PIGA, PHGDH, ACOX1, SFTPB, ZFP57, COQ9, TMEM199, EVC2, NFKB2, ITGA6, PTCH1, EPB42, GCDH, NTRK1, LARGE1, GATM, SNAI2, WDR62, OTC, DLAT, NDUFA2, SLC34A3, POMT2, IRS4, HOGA1, ATR, KLF1, GLUL, NDUFAF4, PAH, SKI, EVC, PNPT1, OPA1, GNE, ALDH3A2, FOXP3, GK, NEUROG3, SCO1, CTH, SMN1, COL6A1, GMPPA, PEX1, BCS1L, FOXC1, FECH, ATP6V1B1, PEX19, CD96, PIGN, CHRNE, ACAD8, SCN8A, NAGLU, NBAS, PIGP, SMPD1, PTS, SLC16A2, TCN2, NARS2, ALG3, THRB, AUH, AGRN, ATP6AP1, AMPD1, WNK1, GALE, PAX6, AKR1D1, FBXL4, MEGF10, PHEX, ABCD3, GNPAT, HPS4, PRKCSH, BIN1, DGUOK, CD3G, EXT2, SLC25A3, CFAP298, PIGT, CDH23, HSD17B10, GORAB, MTMR14, PGAP2, TRAPPC12, ABCG5, CTPS1, PSAT1, PDHX, LCT, GFM1, SCNN1B, PEX6, MAN2B1, SLC6A3, ZAP70, HSD3B2, CEP290, AMACR, FANCA, OGT, PRKAG2, UBR1, ASL, SBDS, ABAT, MYCN, OCRL, CA12, TUBA8, MPDU1, ELANE, DNAI1, IGLL1, PIGU, RARS2, B3GLCT, HSPA9, COA5, F5, IDUA, QDPR, NSD1, PGAP1, AMT, LMBRD1, ABCA12, MCCC2, COG2, BMPR1A, FANCB, PROC, DPM3, FASTKD2, LAMTOR2, DDOST, MC2R, ALG8, SLC37A4, UGT1A1, LIAS, FOXG1, HLCS,

TRMU, GLYCTK, RAF1, SYNE1, SCO2, PRPS1, HGD, STIL, SCNN1A, MOCS2, SLC35A1, NIPBL, GLA, FUCA1, TWNK, CRPPA, NPHP3, WDPCP, SLC25A13, CLN3, PNKP, NPC1, HBB, IGHMBP2, NR3C2, SALL1, RPS19, POMK, TJP2, SERPING1, ACAT1, NDUFA10, JAM3, POLG, SLCO1B1, MTRR, PEPD, PEX10, ALG9, AGA, CHM, SEC63, MMAB, SLC19A3, PTRH2, HMGCS2, ABCC8, COL4A5, HIBCH, DNA2, SLC17A5, MANBA, EIF2B4, SLC6A8, EIF2B3, KBTBD13, PC, TGDS, GALNT3, PCBD1, EYA1, INS, SLC26A2, KCNJ11, OTX2, POGLUT1, SLC35D1, APTX, PCDH19, TRH, AIFM1, CTNS, AGPAT2, TRAPPC9, ASPM, SOX10, NAA10, IL12RB1, PLP1, SLC35C1, B3GAT3, NHEJ1, BICD2, TMIE, GJB6, ATP13A2, SOX2, AKAP9, TNFRSF13B, GALT, SURF1, PEX26, MCPH1, B3GALNT2, SLC25A19, TGM1, VPS13B, MMUT, LIPT1, COQ8A, ASAH1, MUSK, PIGC, MYO15A, ABCD1, SLC39A8, SLC5A5, SPINT2, TRPV4, MLC1, RBM8A, FGG, ST3GAL3, LMNA, BLNK, ALDH7A1, AKT2, CLCN1, DCLRE1C, IVD, ALG1, PHKG2, TH, TTC7A, OPA3, NDUFS2, SEC23B, COG5, ODAD1, GALM, SELENON, SLC52A1, RFXANK, EXOSC3, AP4B1, NGF, ATP7B, GAA, PDSS2, RIT1, BRCA2, NLRP3, ACADSB, RRM2B, TGFBR1, SLC6A1, GP1BB, ORC4, WT1, CD59, HMGCL, ACSF3, INSR, NUBPL, OCLN, SLC35A2, WDR73, CAMTA1, MEF2C, MITF, PPT1, NDUFAF1, SPINK5, HAMP, RYR1, NCF4, GNMT, SLC26A3, VHL, ARSB, ATP7A, STT3B, ORC1, MCEE, PLEC, AGL, FGFR3, COL4A3, RNASET2, RNASEH2C, PAPSS2, MEN1, SIX5, FRAS1, ATP6V1E1, KLHL40, SLC6A5, NDUFAF6, DHCR24, NDUFS7, FBN1, PAX2, ATRX, COG4, KCNH2, HPGD, DPYD, GUSB, TTN, TSPYL1, ALDH5A1, ATP6V0A2, ASPA, FGFR2, KLHL41, MFN2, PGAP3, ATPAF2, MAT1A, CBS, WFS1, ANTXR2, NSDHL, IGF1R, PRDM16, PKD2, PDX1, PCNT, PROP1, SLC16A1, SMAD3, TBL1X, COG8, ATP6V1A, LAMB3, RXYLT1, KLHL7, COQ2, TCIRG1, ANKS6, DOLK, SGSH, CA5A, FANCD2, CHRNA1, PEX3, FARS2, HSPG2, NUS1, ICOS, COL3A1, TMCO1, DYSF, CHAT, STAT1, EEF1A2, DRC1, CDKN1C, DES, JAG1, FAH, AGPS, ITGA7, INVS, MMADHC, PMM2, LFNG, OAT, RFX6, TBCE, CANT1, PRKAR1A, AARS2, GATA1, MEFV, RMND1, TPM3, UNG, MPL, GM2A, SLC10A7, LHX4, UPB1, GFPT1, ARX, MGAT2, MCCC1, SATB2, ZNF423, DMD, CD320, LIPN, ANK1, DNM2, FANCL, CDKL5, ABCA3, COX10, RBBP8, PRODH, PIGO, POLG2, ASNS, XPA, ACTA1, ERCC5, HSPD1, FOXRED1, COX6B1, FANCC, GCSH, GJB4, ALG11, ALAS2, GMPPB, ADAMTSL2, DUOX2, HESX1, EIF2B2, HGF, KCNQ1, MECP2, SUCLG1, DNAH11, SRD5A3, MRPL44, TAT, IL7R, STING1, COX20, COL4A4, POU1F1, CERS3, SPR, BSND, FUT8, JAGN1, CYBB, PTPN11, CYP11B1, SLC52A3, SLC4A1, MED12, SERAC1, RAG1, TNNT1, TUBB2A, FH, SLC7A7, NDUFV2, ADA, EXT1, PNP, PIGG, HPD, GPSM2, ATIC, EIF2AK3, ARG1, GBA, UROD, SUOX, PEX7, CALM1, RAB18, TPM2, GAMT, HNF1B, PIGB, WAS, SPAST, CD247, GAN, GLB1, SCN2A, TIMM50, DDC, AP4S1, MOCS1, AAAS, ASS1, AASS, MCM4, F11, PGM1, GP9, BSCL2, CCDC78, G6PC1, LAMP2, NCF2, ATP1A3, TSC1, DST, ACY1, GALNS, OTOF, SCN1A, SCN5A, SLC19A2, LRRC8A, CYP11B2, HSD3B7, CD40LG, LAMC2, AICDA, COLQ, F10, PEX13, XYLT1, MTHFR, PHOX2B, CHST6, SLC39A4, ETHE1, FADD, POMGNT1, TSFM, ANTXR1, AIMP1, GLRX5, TPP1, TACO1, FBP1, F9, PIGL, ALG12, AVPR2, G6PD, MAP2K2, PEX12, SLC25A1, TMEM70, DNAJC19, GPAA1, AMN, ITGB4, FOLR1, PCCB, MAGT1, SAR1B, TGFBR2, STS, RAC2, HBA1, NPHP1, STXBP1, NDUFA9, JAK3, BTD, KCNT1, LRPPRC, SLC25A22, PCCA, ZEB2, ERCC2, MSMO1, TRAPPC11, IDS, PEX2, DHDDS, CENPJ, USH2A, PSAP, IKBKB, MTTP, PDP1, ETFDH, PURA, ADAR, NLRC4, PSPH, GALK1, D2HGDH, BCAT2, LHX3, SLC45A2, TPRN, HRAS, SLC25A20, SLC6A9, HEXA, LAMA3, COL6A3, PEX5, ATP6AP2, ACVRL1, ITGA2B, DIAPH1, ACADM, TUBB1, LPL, BCAP31, PTPRC, PMP22, SLC3A1, SEC24D

Terminology

Name	Symbol	Description
Zygosity	ZYG	Zygosity describes whether you inherited one copy of this variant from one of your parents (heterozygous), or you inherited two copies from both of your partents (homozygous). Typically for pathogenic variants homozygosity cause a more severe form of the condition. In many cases, heterozygous variants do not lead to the condition becoming apparent in the patient (also known as a recessive condition) but do mean that the next generation is at risk of inheriting the condition (or themselves becoming a carrier).
American College of Medical Genetics	ACMG	The American College of Medical Genetics is an organisation dedicated to the practice of medical genetics. Using a series of factors related to the variant and its context, they have identified the likelihood of a specific variant being causative for a disease. This score is based on a few factors, including allelic frequency (AF) an transcription consequence.
Allelic frequency	AF	Allelic frequency defines how often this variant has been observed in the general population. A very low allelic frequency could potentially be denovo (i.e. it wasn't inherited from either of your parents). Low allelic frequency variants are often considered more likely to be the cause of a negative phenotype or disease.
Autosomal dominant	AD	One mutated copy of the gene in each cell is sufficient for a person to be affected by an autosomal dominant disorder. In some cases, an affected person inherits the condition from an affected parent. In others, the condition may result from a new mutation in the gene and occur in people with no history of the disorder in their family.
Autosomal recessive	AR	In autosomal recessive inheritance, both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition. Autosomal recessive disorders are typically not seen in every generation of an affected family.
X-linked	X-linked dominant	Dominant X-linked dominant disorders are caused by mutations in genes on the X chromosome, one of the two sex chromosomes in each cell. In one of the two sex chromosomes in each cell. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell is sufficient to cause the disorder. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell causes the disorder. In most cases, males experience more severe symptoms of the disorder than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons (no male-to-male transmission).
Y-linked		A condition is considered Y-linked if the mutated gene that causes the disorder is located on the Y chromosome, one of the two sex chromosomes in each of a male's cells. Because only males have a Y chromosome, in Y-linked inheritance, a mutation can only be passed from father to son.
Mitochondrial		Mitochondrial inheritance, also known as maternal inheritance, applies to genes in mitochondrial DNA. Mitochondria, which are structures in each cell that convert molecules into energy, each contain a small amount of DNA. Because only egg cells contribute mitochondria to the developing embryo, only females can pass on mitochondrial mutations to their children. Conditions resulting from mutations in mitochondrial DNA can appear in every generation of a family and can affect both males and females, but fathers do not pass these disorders to their daughters or sons.
Pathogenic		This variant directly contributes to the development of disease. Some pathogenic variants may not be fully penetrant. In the case of recessive or X-linked conditions, a single pathogenic variant may not be sufficient to cause disease on its own. Additional evidence is not expected to alter the classification of this variant.
Likely Pathogenic		There is a high likelihood (greater than 90% certainty) that this variant is disease-causing. Additional evidence is expected to confirm this assertion of pathogenicity, but there is a small chance that new evidence may demonstrate that this variant does not have clinical significance.
Variant Uncertain significance	VUS	There is not enough information at this time to support a more definitive classification of this variant.
Phenotype Name		Phenotype represents the observable characteristics or traits of an organism that are produced by the interaction of the genotype and the environment : the physical expression of one or more genes. Multiple phenotypes can be associated with a single variant.

Name	Symbol	Description
Significance		Significance refers to the standard term used by ClinVar, the internationally recognized database on which this report is based, to classify the types of variants. As the database is a clinical database, the information is clinical and based on an authoritative source when available. The Significance section includes the following standard terms to classify the variants: • **Pathogenic**: A Pathogenic is classified as such if this variant directly contributes to the development of disease. Some pathogenic variants may not be fully penetrant. In the case of recessive or X-linked conditions, a single pathogenic variant may not be sufficient to cause disease on its own. Additional evidence is not expected to alter the classification of this variant. • **Likely Pathogenic**: A Likely Pathogenic variant is classified as such if there is a high likelihood (greater than 90% certainty) that this variant is disease-causing. Additional evidence is expected to confirm this assertion of pathogenicity, but there is a small chance that new evidence may demonstrate that this variant does not have clinical significance. • **Conflicting Interpretations of Pathogenicity**: A Conflicting Interpretations of Pathogenecitity variant is classified as such if it is submitted from a scientific consortium, where groups within the consortium have conflicting interpretations of a variant but provide a single submission to ClinVar. • **Variant of Unknown Significance**: A Variant of Unknown Significance is classified as such if it is there is not enough information at this time to support a more definitive classification of this variant. • **Drug response**: A Drug response variant is classified as such if it represents a complex phenotype that emerges from the interplay of drug-specific genetics, human body, and environmental factors. • **Association**: An association variant is classified as such if there are one or more genotypes within a population co-occur with a phenotypic trait more often than would be expected by chance occurrence.
Review Status		ClinVar reports the level of review supporting the assertion of clinical significance for the variation as review status. Stars provide a graphical representation of the aggregate review status on web pages. Table 1 provides definitions of each review status and the corresponding number of stars. Review status is reported in text format in ClinVar's products available by FTP. A higher number of gold stars corresponds to higher review status. If you wish to get more information about that, please visit ClinVar at the following link: https://www.ncbi.nlm.nih.gov/clinvar/docs/review_status/
HGMD Rankscore		The HGMD computed rankscore is a probability of pathogenicity between 0 and 1, with 1 being most likely disease-causing compared to other HGMD entries. The score is computed using a machine learning approach, and is based upon multiple lines of evidence, including HGMD literature support for pathogenicity, evolutionary conservation (100 way vertebrate alignment), variant allele frequency and in-silico pathogenicity prediction.
HGMD Variant Class		**DM:** Pathological mutation reported to be disease-causing in the corresponding literature report (majority of HGMD data). **DM?:** Likely pathological mutation reported to be disease-causing in the corresponding report, but where the author has indicated that there may be some degree of doubt, or subsequent evidence has come to light in the literature, calling the deleterious nature of the variant into question. **DF:** A polymorphism reported to be in significant association with a disease/phenotype ($p<0.05$) that is assumed to be functional (e.g. as a consequence of location, evolutionary conservation, replication studies etc.), although there may as yet be no direct evidence (e.g. from an expression study) of a functional effect. **DFP:** A polymorphism reported to be in significant association with disease ($p<0.05$) that has evidence of being of direct functional importance (e.g. as a consequence of altered gene expression, mRNA studies etc). **FP:** A polymorphism reported to affect the structure, function or expression of the gene (or gene product), but with no disease association reported as yet. **R:** A variant entry retired from HGMD due to being found to have been erroneously included ab initio, or variant that has been subjected to correction in the literature resulting in the record becoming obsolete, merged or otherwise invalid.

Methods

Versions

VCF Version: UZrSsgMIMcGhIW_Mp0vp4vVsitnPp.cC
Clinvar Database Version: FgUM_0StTQ4PCkHW_E7OkqqE0l.5KRqI

Extraction

Before sequencing, DNA extraction and library preparation processes were carried-out by automated liquid handling robots. Sequencing was completed using the NovaSeq 6000 instrument (Illumina).

The Nextera DNA Flex (Illumina) library was used during sequencing.

Analysis

Primary and secondary analysis was performed on the Illumina DRAGEN platform. Our secondary analysis extends the GATK "best practices" pipeline. This includes Variant Quality Score Recalibration

It is important to note that applying a filter will not remove any data from the VCF file; it will just annotate the "FILTER" column. Variants with the "PASS" annotation are considered high quality and may, therefore, be used for advanced downstream analysis.

Sequence data is primarily aligned to the GATK GRCh37 reference genome and mitochondria is aligned to the Revised Cambridge Reference Sequence (NC_012920.1). Additional references may have been requested though tertiary analysis is not conducted on variant calls using references other than GRCh37.

Limitations

Test results are not interpretations. All variants reported in the genes included in the panel are reported.

Rare polymorphisms may lead to false-negative or false-positive results.

Due to limited read length and other contributing technical limitations, repeat expansions (e.g. in the Huntington gene, the SCA-genes, the myotonic dystrophy repeat region, and other similar regions) cannot be assessed with the applied method

This report is based on SNP VCF data.

Disclaimer

Any preparation and processing of a sample from saliva collection kit to Dante Labs by a customer is assumed to belong to the email used by the customer at the moment of kit registration on the Dante Labs Genome Manager platform before the shipment of the specimen to the laboratory.

The analysis and reporting conducted by Dante Labs are based on information from one or more published third-party scientific and medical studies.

Because of scientific and medical information changes over time, your risk assessment for one or more of the conditions contained within this report may also change over time. For example, opinions differ on the importance and relative weights given to genetic factors. Also, epidemiological data isn't available for some conditions, and this report may not be able to provide definitive information about the severity of a particular condition. We recommend asking your healthcare provider to correctly interpret them. Therefore, this report may not be 100% accurate (e.g., new research could mean different results) and may not predict actual results or outcomes.

This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The US Food and Drug Administration (FDA) has determined that clearance or approval of this method is not necessary and thus neither have been obtained.

Contact

Please contact contact@dantelabs.com for more information on the contents of this report, our analysis methodology, and the limitations of this process.

Doctor's Signature

Signature

Date