Helix Comprehensive Carrier Screen

Item	Description
Test Name	Helix Comprehensive Carrier Screen
Test Type	Carrier Screening
Catalog Number	CCRF1
Procedure Code	H000125-7
Test Description	This panel evaluates 278 genes (females) or 257 (males) associated with autosomal recessive and X-linked inherited disorders. X-linked disorders are not included when the test is ordered for biological males.
Genes Tested	*ABCA3, ABCC8, ABCD1, ACADM, ACADS, ACADVL, ACAT1, ADA, ADAMTS2, AGA, AGL, AGXT, AHI1, AIRE, ALDH3A2, ALDOB, ALG6, ALMS1, ALPL, AMT, ANO10, ARG1, ARSA, ARSB, ARX, ASL, ASNS, ASPA, ASS1, ATM, ATP6V1B1, ATP7A, ATP7B, BBS1, BBS10, BBS12, BBS2, BCKDHA, BCKDHB, BCS1L, BLM, BTD, CAPN3, CBS, CC2D2A, CCDC88C, CDH23, CEP290, CERKL, CFTR, CHM, CHRNE, CLCN1, CLN3, CLN5, CLN6, CLN8, CLRN1, CNGB3, COL4A3, COL4A4, COL4A5, COL7A1, CPS1, CPT1A, CPT2, CRYL1, CTNS, CTSK, CYBA, CYP11A1, CYP11B1, CYP11B2, CYP21A2, CYP27A1, CYP27B1, DBT, DCLRE1C, DHCR7, DHDDS, DLD, DMD, DNAH5, DNAI1, DNAI2, DPYD, DYNC2H1, DYSF, ELP1, ERCC2, ERCC6, ERCC8, ETHE1, EVC, EVC2, EYS, F11, F9, FAH, FAM161A, FANCA, FANCC, FKRP, FKTN, FMO3, FMR1, G6PC, GAA, GALC, GALK1, GALNS, GALT, GAMT, GBA, GBE1, GCDH, GJB1, GJB2, GJB6, GLA, GLB1, GLDC, GLE1, GNE, GNPTAB, GNPTG, GNS, GRHPR, GRIP1, GUSB, HADHA, HBA1, HBA2, HBB, HEXA, HEXB, HGD, HGSNAT, HLCS, HMGCL, HOGA1, HPS1, HPS3, HSD17B4, HYLS1, IDS, IDUA, IL2RG, IVD, KCNJ11, L1CAM, LAMA2, LAMA3, LAMB3, LAMC2, LIPA, LOXHD1, LRP2, LRPPRC, MAN2B1, MCCC1, MCCC2, MCOLN1, MCPH1, MED17, MEFV, MESP2, MID1, MLC1, MMAA, MMAB, MMACHC, MUT, MPL, MTHFR, MTM1, MTTP, MVK, MYO7A, NAGA, NAGLU, NBN, NDUFAF5, NDUFS4, NDUFS6, NEB, NPC1, NPC2, NPHS1, NPHS2, NR0B1, NR2E3, NTRK1, OAT, OCA2, OPA3, OTC, PAH, PC, PCCA, PCCB, PCDH15, PDHA1, PEX1, PEX10, PEX12, PEX2, PEX26, PEX6, PEX7, PFKM, PHGDH, PKHD1, PLP1, PMM2, POLG, POMGNT1, PPT1, PRF1, PROP1, PTS, PUS1, PYGM, RAG1, RAG2, RAPSN, RARS2, RMRP, RNASEH2B, RPE65, RS1, RTEL1, SACS, SCO2, SEPSECS, SGCA, SGCB, SGCD, SGCG, SGSH, SLC12A6, SLC17A5, SLC19A3, SLC22A5, SLC25A13, SLC25A20, SLC26A2, SLC26A4, SLC35A3, SLC37A4, SLC6A8, SLC7A7, SMN1, SMPD1, STAR, SUMF1, SURF1, TAT, TCIRG1, TECPR2, TF, TGM1, TH, TMEM216, TPP1, TRMU, TTPA, TYMP, USH1C, USH2A, VPS13A, VPS13B, VRK1, VSX2, WNT10A, XPA, XPC, ZFYVE26*
Genetics Information	This test utilizes next-generation sequencing to detect single nucleotide variants, insertions and deletions up to 20 bp, and copy number variants in genes associated with autosomal recessive and X-linked inherited disorders.
Indications For Testing	Prenatal or preconception risk assessment for individuals who are pregnant or planning to conceive
Clinical Descriptions	This panel includes genes that have an established association with the autosomal recessive or X-linked conditions described below.

Item	Description
Interpretation	Variants are interpreted manually using locus-specific databases, literature searches, and other molecular biological principles. Variants classified as pathogenic, likely pathogenic, or risk allele which are located in the coding regions and nearby intronic regions (+/- 20 bp) of the genes listed are reported. Variants of uncertain significance (VUSes) are not reported.
Reclassification Of Variants	Past classifications are not revised for carrier tests.
Variant Evaluation	Variant classification is performed using the guidelines set forth by the American College of Medical Genetics and Genomics and the Association for Molecular Pathology, with modifications as suggested by domain specific Expert Panels of the Clinical genome Resource (ClinGen) when available. Variant pathogenicity is categorized as benign, likely benign, variant of uncertain significance (VUS), likely pathogenic, or pathogenic. Distinct from this 5-tier system, FMR1 trinucleotide repeat expansions are classified by repeat size in accordance with ACMG technical standards as Normal, Intermediate, Premutation, or Full Mutation. Alleles are categorized as Normal (< 45 repeats), Intermediate (45-54 repeats), Premutation (55-200 repeats), or Full Mutation (> 200 repeats), consistent with current ACMG technical standards for Fragile X syndrome.
Turnaround Time - Standard	Typically 7 to 21 days
Turnaround Time - Requery (SOQO®)	Typically 7 to 21 days
Available In NY State	Yes
Test Classification	This test was developed, and its performance characteristics determined, by Fulgent Therapeutics LLC in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.
Performing Laboratory Information	Fulgent Therapeutics LLC CLIA Laboratory Number: 05D2043189 Laboratory Hours of Operation: Monday-Friday (7AM-5PM PST) Saturday (8AM-3PM PST) Address: 4399 Santa Anita Ave., El Monte, CA 91731 Healthcare professionals may contact Helix directly to discuss results: Helix Customer Service: (844) 211-2070 Email: clinicalsupport@helix.com
Regulatory Information	CLIA Complexity: High Test Classification: Non-Waived/ Laboratory Developed Test
CLIA Category	Chemistry / Routine Chemistry

Conditions for Helix Comprehensive Carrier Screen

- *(ABCA3)* Surfactant metabolism dysfunction, pulmonary 3
- *(ABCC8)* Familial hyperinsulinism
- *(ABCD1)* Adrenoleukodystrophy, X-linked
- *(ACADM)* Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency
- *(ACADS)* Short-chain acyl-coA dehydrogenase (SCAD) deficiency
- *(ACADVL)* Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency
- *(ACAT1)* 3-ketothiolase deficiency
- *(ADA)* Adenosine deaminase deficiency
- *(ADAMTS2)* Ehlers-Danlos syndrome, dermatosparaxis type
- *(AGA)* Aspartylglucosaminuria
- *(AGL)* Glycogen storage disease type III
- *(AGXT)* Primary hyperoxaluria type 1
- *(AHI1)* Joubert syndrome, AHI1-related
- *(AIRE)* Autoimmune polyendocrinopathy syndrome type I
- *(ALDH3A2)* Sjogren-Larsson syndrome
- *(ALDOB)* Hereditary fructose intolerance
- *(ALG6)* Congenital disorder of glycosylation type Ic
- *(ALMS1)* Alstrom syndrome
- *(ALPL)* Hypophosphatasia
- *(AMT)* Glycine encephalopathy
- *(ANO10)* Spinocerebellar ataxia 10
- *(ARG1)* Arginase deficiency
- *(ARSA)* Metachromatic leukodystrophy
- *(ARSB)* Mucopolysaccharidosis type VI (Maroteaux-Lamy syndrome)
- *(ARX)* X-linked intellectual disability, ARX-related
- *(ASL)* Argininosuccinate lyase deficiency
- *(ASNS)* Asparagine synthetase deficiency
- *(ASPA)* Canavan disease
- *(ASS1)* Citrullinemia
- *(ATM)* Ataxia-telangiectasia
- *(ATP6V1B1)* Renal tubular acidosis with deafness
- *(ATP7A)* Menkes disease
- *(ATP7B)* Wilson disease
- *(BBS1)* Bardet-Biedl syndrome type 1
- *(BBS10)* Bardet-Biedl syndrome type 10
- *(BBS12)* Bardet-Biedl syndrome type 12
- *(BBS2)* BBS2-related ciliopathies
- *(BCKDHA)* Maple syrup urine disease type Ia
- *(BCKDHB)* Maple syrup urine disease type Ib
- *(BCS1L)* Mitochondrial complex III deficiency
- *(BLM)* Bloom syndrome
- *(BTD)* Biotinidase deficiency
- *(CAPN3)* Limb-girdle muscular dystrophy type 2A
- *(CBS)* Homocystinuria due to cystathionine beta-synthase deficiency
- *(CC2D2A)* Joubert syndrome 9
- *(CCDC88C)* Congenital hydrocephalus 1
- *(CDH23)* Usher syndrome, type 1D
- *(CEP290)* CEP290-related Ciliopathies
- *(CERKL)* Retinitis pigmentosa 26
- *(CFTR)* Cystic Fibrosis
- *(CHM)* Choroideremia
- *(CHRNE)* Congenital myasthenic syndrome
- *(CLCN1)* Autosomal recessive congenital myotonia
- *(CLN3)* Neuronal ceroid lipofuscinosis
- *(CLN5)* Neuronal ceroid lipofuscinosis 5
- *(CLN6)* Neuronal ceroid lipofuscinosis, CLN6-related
- *(CLN8)* Neuronal ceroid lipofuscinosis, CLN8-related
- *(CLRN1)* Usher syndrome, type 3A
- *(CNGB3)* Achromatopsia
- *(COL4A3)* Alport syndrome, COL4A3-related
- *(COL4A4)* Alport syndrome, COL4A4-related
- *(COL4A5)* Alport syndrome, COL4A5-related
- *(COL7A1)* Dystrophic epidermolysis bullosa
- *(CPS1)* Carbamoylphosphate synthetase I deficiency
- *(CPT1A)* Carnitine palmitoyltransferase IA deficiency
- *(CPT2)* Carnitine palmitoyltransferase II deficiency
- *(CTNS)* Cystinosis
- *(CTSK)* Pycnodysostosis
- *(CYBA)* Chronic granulomatous disease
- *(CYP11A1)* Congenital adrenal insufficiency
- *(CYP11B1)* Congenital adrenal hyperplasia due to 11-beta-hydroxylase deficiency
- *(CYP11B2)* Corticosterone methyloxidase deficiency
- *(CYP21A2)* Congenital adrenal hyperplasia due to 21-hydroxylase deficiency
- *(CYP27A1)* Cerebrotendinous xanthomatosis
- *(CYP27B1)* Vitamin D-dependent rickets, type 1
- *(DBT)* Maple syrup urine disease, type II
- *(DCLRE1C)* Severe combined immunodeficiency with sensitivity to ionizing radiation
- *(DHCR7)* Smith-Lemli-Opitz syndrome
- *(DHDDS)* Retinitis pigmentosa 59

Conditions for Helix Comprehensive Carrier Screen

- *(DLD)* Dihydrolipoamide dehydrogenase deficiency
- *(DMD)* Dystrophinopathies
- *(DNAH5)* Primary ciliary dyskinesia, DNAH5-related
- *(DNAI1)* Primary ciliary dyskinesia, DNAI1-related
- *(DNAI2)* Primary ciliary dyskinesia, DNAI2-related
- *(DPYD)* Dihydropyrimidine dehydrogenase deficiency
- *(DYNC2H1)* Short-rib thoracic dysplasia 3 with or without polydactyly
- *(DYSF)* Limb-girdle muscular dystrophy type 2B
- *(ELP1)* Familial Dysautonomia
- *(ERCC2)* ERCC2-related disorders
- *(ERCC6)* ERCC6-related disorders
- *(ERCC8)* Cockayne syndrome type A
- *(ETHE1)* Ethylmalonic encephalopathy
- *(EVC)* EVC-related bone growth disorders
- *(EVC2)* EVC2-related bone growth disorders
- *(EYS)* Retinitis pigmentosa 25
- *(F11)* Factor XI deficiency
- *(F9)* Hemophilia B
- *(FAH)* Tyrosinemia, type 1
- *(FAM161A)* Retinitis pigmentosa 28
- *(FANCA)* Fanconi anemia group A
- *(FANCC)* Fanconi anemia group C
- *(FKRP)* FKRP Alpha-dystroglycanopathies-
- *(FKTN)* FKTN Alpha-dystroglycanopathies
- *(FMO3)* Trimethylaminuria
- *(FMR1)* Fragile X Syndrome
- *(G6PC)* Glycogen storage disease, type Ia
- *(GAA)* Pompe disease
- *(GALC)* Krabbe disease
- *(GALK1)* Galactokinase deficiency
- *(GALNS)* Mucopolysaccharidosis IVA (Morquio syndrome A)
- *(GALT)* Galactosemia
- *(GAMT)* Guanidinoacetate methyltransferase deficiency
- *(GBA)* Gaucher disease
- *(GBE1)* Glycogen storage disease IV
- *(GCDH)* Glutaric aciduria, type I
- *(GJB1)* Charcot-Marie-Tooth disease, X-linked type 1
- *(GJB2, GJB6, CRYL1)* Nonsyndromic hearing loss 1A
- *(GLA)* Fabry disease
- *(GLB1)* GLB1-related gangliosidoses
- *(GLDC)* Glycine encephalopathy, GLDC-related
- *(GLE1)* Lethal congenital contracture syndrome 1
- *(GNE)* Inclusion body myopathy type 2 (Nonaka myopathy)
- *(GNPTAB)* Mucolipidosis II & III
- *(GNPTG)* Mucolipidosis III gamma
- *(GNS)* Mucopolysaccharidosis IIID (Sanfilippo syndrome D)
- *(GRHPR)* Primary hyperoxaluria type II
- *(GRIP1)* Fraser syndrome
- *(GUSB)* Mucopolysaccharidosis type VII
- *(HADHA)* Trifunctional protein deficiency
- *(HBA1)* Alpha thalassemia
- *(HBA2)* Alpha thalassemia
- *(HBB)* Sickle cell disease, Hemoglobin C disease, Beta thalassemia
- *(HEXA)* Tay-Sachs disease
- *(HEXB)* Sandhoff disease
- *(HGD)* Alkaptonuria
- *(HGSNAT)* Mucopolysaccharidosis type IIIC (Sanfilippo syndrome C)
- *(HLCS)* Holocarboxylase synthetase deficiency
- *(HMGCL)* 3-hydroxy-3-methylglutaryl-CoA lyase deficiency
- *(HOGA1)* Primary hyperoxaluria type III
- *(HPS1)* Hermansky-Pudlak syndrome 1
- *(HPS3)* Hermansky-Pudlak syndrome 3
- *(HSD17B4)* D-bifunctional protein deficiency
- *(HYLS1)* Hydrolethalus syndrome
- *(IDS)* Mucopolysaccharidosis type II (Hunter syndrome)
- *(IDUA)* Mucopolysaccharidosis, type I (Hurler syndrome)
- *(IL2RG)* X-linked severe combined immunodeficiency
- *(IVD)* Isovaleric Acidemia
- *(KCNJ11)* KCNJ11-related hyperinsulinism
- *(L1CAM)* L1 syndrome
- *(LAMA2)* Muscular dystrophy, LAMA2-related
- *(LAMA3)* Junctional epidermolysis bullosa 2
- *(LAMB3)* Junctional epidermolysis bullosa, LAMB3-related
- *(LAMC2)* Junctional epidermolysis bullosa, LAMC2-related
- *(LIPA)* Lysosomal acid lipase deficiency
- *(LOXHD1)* Nonsyndromic hearing loss 77
- *(LRP2)* Donnai-Barrow syndrome
- *(LRPPRC)* Leigh syndrome with Complex IV deficiency
- *(MAN2B1)* Alpha-Mannosidosis
- *(MCCC1)* 3-Methylcrotonyl-CoA carboxylase 1 deficiency (3-MCC deficiency)

Conditions for Helix Comprehensive Carrier Screen

- *(MCCC2)* 3-Methylcrotonyl-CoA carboxylase 2 deficiency (3-MCC deficiency)
- *(MCOLN1)* Mucolipidosis IV
- *(MCPH1)* Primary microcephaly 1, recessive
- *(MED17)* Postnatal Progressive Microcephaly with Seizures and Brain Atrophy
- *(MEFV)* Familial Mediterranean fever
- *(MESP2)* Spondylocostal dysostosis
- *(MID1)* Opitz GBBB syndrome, type I
- *(MLC1)* Megalencephalic leukoencephalopathy with subcortical cysts
- *(MMAA)* Methylmalonic aciduria, cblA type
- *(MMAB)* Methylmalonic aciduria, cblB type
- *(MMACHC)* Methylmalonic aciduria and homocystinuria, cblC type
- *(MPL)* Congenital amegakaryocytic thrombocytopenia
- *(MTHFR)* Homocystinuria, MTHFR-related
- *(MTM1)* Myotubular myopathy, X-linked
- *(MTTP)* Abetalipoproteinemia
- *(MUT)* Methylmalonic aciduria- methylmalonyl-CoA mutase deficiency
- *(MVK)* Mevalonate kinase deficiency
- *(MYO7A)* MYO7A-related disorders
- *(NAGA)* Schindler disease types 1 and 3
- *(NAGLU)* Mucopolysaccharidosis type IIIB (Sanfilippo syndrome B)
- *(NBN)* Nijmegen breakage syndrome
- *(NDUFAF5)* Mitochondrial complex I deficiency (Leigh syndrome)
- *(NDUFS4)* Mitochondrial complex I deficiency
- *(NDUFS6)* Mitochondrial complex I deficiency (Leigh syndrome)
- *(NEB)* Nemaline myopathy
- *(NPC1)* Niemann-Pick disease, type C1
- *(NPC2)* Niemann-Pick disease, type C2
- *(NPHS1)* Congenital nephrotic syndrome, type 1
- *(NPHS2)* Congenital nephrotic syndrome, type 2
- *(NR0B1)* Congenital adrenal hypoplasia, X-linked
- *(NR2E3)* NR2E3-related retinal dystrophies
- *(NTRK1)* Congenital insensitivity to pain with anhidrosis
- *(OAT)* Gyrate atrophy of choroid and retina
- *(OCA2)* Oculocutaneous albinism type II
- *(OPA3)* Costeff syndrome
- *(OTC)* Ornithine transcarbamylase deficiency
- *(PAH)* Phenylalanine Hydroxylase deficiency (Phenylketonuria)
- *(PC)* Pyruvate carboxylase deficiency
- *(PCCA)* Propionic acidemia, PCCA-related
- *(PCCB)* Propionic acidemia, PCCB-related
- *(PCDH15)* PCDH15-related sensory loss
- *(PDHA1)* Pyruvate dehydrogenase E1-alpha deficiency
- *(PEX1)* Zellweger syndrome, PEX1-related
- *(PEX10)* Zellweger syndrome, PEX10-related
- *(PEX12)* Zellweger syndrome, PEX12-related
- *(PEX2)* Zellweger syndrome, PEX2-related
- *(PEX26)* Zellweger syndrome
- *(PEX6)* Zellweger syndrome, PEX6-related
- *(PEX7)* Rhizomelic chondrodysplasia punctata, type 1
- *(PFKM)* Glycogen storage disease VII
- *(PHGDH)* Phosphoglycerate dehydrogenase deficiency
- *(PKHD1)* Polycystic kidney disease, PKHD1-related
- *(PLP1)* PLP1-related disorders
- *(PMM2)* Congenital disorder of glycosylation type Ia
- *(POLG)* POLG-related disorders
- *(POMGNT1)* POMGNT1 Alpha-dystroglycanopathies
- *(PPT1)* Neuronal ceroid lipofuscinosis, PPT1-related
- *(PRF1)* Hemophagocytic lymphohistiocytosis familial, 2
- *(PROP1)* Combined pituitary hormone deficiency 2
- *(PTS)* Tetrahydrobiopterin deficiency
- *(PUS1)* Mitochondrial myopathy and sideroblastic anemia 1
- *(PYGM)* Glycogen storage disease type V
- *(RAG1)* Omenn syndrome, RAG1-related
- *(RAG2)* Omenn syndrome, RAG2-related
- *(RAPSN)* RAPSN-associated acetylcholine receptor deficiency
- *(RARS2)* Pontocerebellar hypoplasia type 6
- *(RMRP)* Cartilage-Hair Hypoplasia Anauxetic Dysplasia Spectrum Disorder
- *(RNASEH2B)* Aicardi Goutieres syndrome 2
- *(RPE65)* RPE65-related retinopathy
- *(RS1)* Juvenile retinoschisis, X-linked
- *(RTEL1)* Dyskeratosis congenita type 5
- *(SACS)* Autosomal recessive spastic ataxia of Charlevoix-Saguenay
- *(SCO2)* Mitochondrial complex IV deficiency
- *(SEPSECS)* Pontocerebellar hypoplasia type 2D
- *(SGCA)* Limb-girdle muscular dystrophy, type 2D
- *(SGCB)* Limb-girdle muscular dystrophy, type 2E
- *(SGCD)* Limb-girdle muscular dystrophy, type 2F

- *(SGCG)* Limb-girdle muscular dystrophy, type 2C
- *(SGSH)* Mucopolysaccharidosis IIIA (Sanfilippo syndrome A)
- *(SLC12A6)* Andermann syndrome
- *(SLC17A5)* Sialic acid storage disorder
- *(SLC19A3)* Biotin-responsive basal ganglia disease
- *(SLC22A5)* Systemic primary carnitine deficiency
- *(SLC25A13)* Citrin deficiency
- *(SLC25A20)* Carnitine-acylcarnitine translocase deficiency
- *(SLC26A2)* SLC26A2-related disorders
- *(SLC26A4)* Pendred syndrome
- *(SLC35A3)* Arthrogryposis, intellectual disability. and seizures
- *(SLC37A4)* Glycogen storage disease, type Ib
- *(SLC6A8)* Creatine deficiency syndrome
- *(SLC7A7)* Lysinuric protein intolerance
- *(SMN1)* Spinal muscular atrophy
- *(SMPD1)* Niemann-Pick disease, type A/B
- *(STAR)* Lipoid congenital adrenal hyperplasia
- *(SUMF1)* Multiple sulfatase deficiency
- *(SURF1)* Leigh syndrome, SURF1-related
- *(TAT)* Tyrosinemia, type II
- *(TCIRG1)* Osteopetrosis 1
- *(TECPR2)* Spastic paraplegia 49
- *(TF)* Atransferrinemia
- *(TGM1)* Congenital ichthyosis
- *(TH)* Segawa syndrome
- *(TMEM216)* TMEM216-related ciliopathies
- *(TPP1)* Neuronal ceroid lipofuscinosis, TPP1-related
- *(TRMU)* Liver failure, acute infantile
- *(TTPA)* Ataxia with isolated vitamin E deficiency
- *(TYMP)* Mitochondrial neurogastrointestinal encephalopathy (MNGIE) disease
- *(USH1C)* USH1C-related disorders
- *(USH2A)* Usher syndrome, type 2A
- *(VPS13A)* Choreoacanthocytosis
- *(VPS13B)* Cohen syndrome
- *(VRK1)* Pontocerebellar hypoplasia type 1A
- *(VSX2)* Microphthalmia with or without coloboma
- *(WNT10A)* WNT10A-related ectodermal dysplasias
- *(XPA)* Xeroderma pigmentosum, group A
- *(XPC)* Xeroderma pigmentosum, group C
- *(ZFYVE26)* Spastic paraplegia 15

Genomic DNA was isolated from the submitted specimen indicated above (if cellular material was submitted). DNA was barcoded, and enriched for the coding exons of targeted genes using hybrid capture technology. Prepared DNA libraries were then sequenced using a Next Generation Sequencing technology. Following alignment to the human genome reference sequence (assembly GRCh37), variants were detected in regions of at least 10x coverage. For this specimen, 99.66% and 99.61% of coding regions and splicing junctions of genes listed had been sequenced with coverage of at least 10x and 20x, respectively, by NGS or by Sanger sequencing. The remaining regions did not have 10x coverage, and were not evaluated. Variants were interpreted manually using locus specific databases, literature searches, and other molecular biological principles. To minimize false positive results, any variants that do not meet internal quality standards are confirmed by Sanger sequencing. Variants classified as pathogenic, likely pathogenic, or risk allele which are located in the coding regions and nearby intronic regions (+/- 20bp) of the genes listed above are reported. Variants outside these intervals may be reported but are typically not guaranteed. When a single pathogenic or likely pathogenic variant is identified in a clinically relevant gene with autosomal recessive inheritance, the laboratory will attempt to ensure 100% coverage of coding sequences either through NGS or Sanger sequencing technologies ("fill-in"). All genes listed were evaluated for large deletions and/or duplications. However, single exon deletions or duplications will not be detected in this assay, nor will copy number alterations in regions of genes with significant pseudogenes. Putative deletions or duplications are analyzed using Fulgent Germline proprietary pipeline for this specimen. Bioinformatics: The Fulgent Germline v2019.2 pipeline was used to analyze this specimen.

These test results and variant interpretation are based on the proper identification of the submitted specimen, accuracy of any stated familial relationships, and use of the correct human reference sequences at the queried loci. In very rare instances, errors may result due to mix-up or co-mingling of specimens. Positive results do not imply that there are no other contributors, genetic or otherwise, to future pregnancies, and negative results do not rule out the genetic risk to a pregnancy. Official gene names change over time. Fulgent uses the most up to date gene names based on HUGO Gene Nomenclature Committee (https://www.genenames.org) recommendations. If the gene name on report does not match that of ordered gene, please contact the laboratory and details can be provided. Result interpretation is based on the available clinical and family history information for this individual, collected published information, and Alamut annotation available at the time of reporting. This assay is not designed or validated for the detection of low-level mosaicism or somatic mutations. This assay will not detect certain types of genomic aberrations such as translocations, inversions, or repeat expansions other than specified genes. DNA alterations in regulatory regions or deep intronic regions (greater than 20bp from an exon) may not be detected by this test. Unless otherwise indicated, no additional assays have been performed to evaluate genetic changes in this specimen. There are technical limitations on the ability of DNA sequencing to detect small insertions and deletions. Our laboratory uses a sensitive detection algorithm, however these types of alterations are not detected as reliably as single nucleotide variants. Rarely, due to systematic chemical, computational, or human error, DNA variants may be missed. Although next generation sequencing technologies and our bioinformatics analysis significantly reduce the confounding contribution of pseudogene sequences or other highly-homologous sequences, sometimes these may still interfere with the technical ability of the assay to identify pathogenic alterations in both sequencing and deletion/duplication analyses. Deletion/duplication analysis can identify alterations of genomic regions which include one whole gene (buccal swab specimens and whole blood specimens) and are two or more contiguous exons in size (whole blood specimens only); single exon deletions or duplications may occasionally be identified, but are not routinely detected by this test. When novel DNA duplications are identified, it is not possible to discern the genomic location or orientation of the duplicated segment, hence the effect of the duplication cannot be predicted. Where deletions are detected, it is not always possible to determine

whether the predicted product will remain in-frame or not. Unless otherwise indicated, deletion/duplication analysis has not been performed in regions that have been sequenced by Sanger.

Gene Specific Notes:

BTD: If detected, the variant NM_001370658.1:c.1270G>C (p.Asp424His) will not be reported as this variant is associated with low disease penetrance and is primarily associated with reduced enzyme activity when homozygous. CFTR: Analysis of the intron 8 polymorphic region (e.g. IVS8-5T allele) is only performed if the p.Arg117His (R117H) mutation is detected. Single exon deletion/duplication analysis is limited to deletions of previously reported exons: 1, 2, 3, 11, 19, 20, 21. CFTR variants primarily associated with CFTR-related isolated congenital bilateral absence of the vas deferens and CFTR-related pancreatitis are not included in this analysis. CFTR variants with insufficient evidence of being cystic fibrosis mutations will not be reported either. CRYL1: This gene is only included for whole gene deletions related to GJB2-related hearing loss. CYP21A2: Significant pseudogene interference and/or reciprocal exchanges between the CYP21A2 gene and its pseudogene, CYP21A1P, have been known to occur and may impact results. As such, the relevance of variants reported in this gene must be interpreted clinically in the context of the clinical findings, biochemical profile, and family history of each patient. CYP21A2 variants primarily associated with non-classic congenital adrenal hyperplasia (CAH) are not included in this analysis (PubMed: 23359698). The variants associated with non-classic disease, including but not limited to c.188A>T (p.His63Leu), c.844G>T (p.Val282Leu), c.1174G>A (p.Ala392Thr), and c.1360C>T (p.Pro454Ser) will not be reported. LR-PCR is not routinely ordered for NM_000500.9:c.955C>T (p.Gln319Ter). Individuals with c.955C>T (p.Gln319Ter) will be reported as a Possible Carrier indicating that the precise nature of the variant has not been determined by LR-PCR and that the variant may occur in the CYP21A2 wild-type gene or in the CYP21A1P pseudogene. The confirmation test is recommended if the second reproductive partner is tested positive for variants associated with classic CAH. DMD: Single exon deletion/duplication analysis is limited to exons with >1 patient reported in the UMD database (http://www.umd.be/DMD/W_DMD/index.html), accessed Dec 29,2020 and all out-of-frame exons after exon 3. This includes deletion of exon 1, and duplication of exon 2, and del/dup for exons 3, 6~8, 11, 12, 17~22, 43~46, 48, 50~56, 58~63, 65~70, 75, 76, and 78. Single-exon detection is limited to blood samples. FMR1: The exact size of alleles >200 CGG repeats cannot be determined; these alleles are pathogenic for X-Linked Fragile X Syndrome. Alleles with <10 repeats may fail to amplify; these alleles are benign. The repeat length for this gene may vary by +/- 1 repeat unit. Methylation is not analyzed. RP-PCR analysis of the FMR1 promoter is not routinely performed in males. Small degrees of size mosaicism, including gonadal mosaicism, may not be detected. GALT: The D2 "Duarte" allele is not included in this analysis. While this allele can cause positive newborn screening results, it is not known to cause clinical symptoms in any state (PubMed: 25473725, 30593450). GBA: The current testing method may not be able to reliably detect certain pathogenic variants in the GBA gene due to homologous recombination between the pseudogene and the functional gene. GJB6: This gene is only included for whole gene deletions related to GJB2-related hearing loss. MTHFR: As recommended by ACMG, the two common polymorphisms in the MTHFR gene - c.1286A>C (p.Glu429Ala, also known as c.1298A>C) and c.665C>T (p.Ala222Val, also known as c.677C>T) - are not reported in this test due to lack of sufficient clinical utility to merit testing (PubMed: 23288205). NPHS2: If detected, the variant NM_014625.3:c.686G>A(p.Arg229Gln) will not be reported as this variant is not significantly associated with disease when homozygous or in the compound heterozygous state with variants in exons 1-6 of NPHS2. SMN1: The current testing method detects sequencing variants in exon 7 and copy number variations in exons 7-8 of the SMN1 gene (NM_022874.2). Sequencing and deletion/duplication analysis are not performed on any other region in this gene. About 5%-8% of the population have two copies of SMN1 on a single chromosome and a deletion on the other chromosome, known as a [2+0] configuration (PubMed: 20301526). The current testing method cannot directly detect carriers with a [2+0] SMN1 configuration, but can detect linkage between the silent carrier allele and certain

population-specific single nucleotide changes. As a result, a negative result for carrier testing greatly reduces but does not eliminate the chance that a person is a carrier. Only abnormal results will be reported. WNT10A: If detected, certain common variants which are associated with autosomal dominant selective tooth agenesis are not reported. These variants are associated with low penetrance for autosomal recessive disease and are commonly found as homozygous in healthy controls.

Disclaimer:
This test was developed, performed, and its performance characteristics determined by Fulgent Therapeutics LLC (CAP# 8042697, CLIA# 05D2043189), 4399 Santa Anita Ave., El Monte, CA 91731. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. Since genetic variation, as well as systematic and technical factors, can affect the accuracy of testing, the results of testing should always be interpreted in the context of clinical and familial data. For assistance with interpretation of these results, healthcare professionals may contact us directly at 844-211-2070 or by email at clinicalsupport@helix.com. It is recommended that patients receive appropriate genetic counseling to explain the implications of the test result, including its residual risks, uncertainties and reproductive or medical options.

Targeted Genes & Methodology for Helix Comprehensive Carrier Screen

The following applies to the Helix Comprehensive Carrier Screen. Testing is performed to evaluate for the presence of variants in coding regions and extending to +/- 20 base pairs of adjacent intronic sequences on either side of the coding exons of the genes analyzed. In addition, the analysis will cover select non-coding variants, as listed below. Next-generation sequencing is performed to test for the presence of small variants and copy number variants in the genes analyzed. Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

This list is current from December 2025 to the present. This document is intended to highlight additional evaluations for variants of high clinical interest as well as technical limitations. For questions regarding genes, reference transcripts, or specific regions covered, contact Helix Customer Service at (844) 211-2070.

Genomic Build: GRCh37
Catalog Number: CCRF1

Gene	Transcript	Technical Limitations
ABCA3	NM_001089.3	
ABCC8	NM_000352.6	
ABCD1	NM_000033.4	
ACADM	NM_000016.6	
ACADS	NM_000017.4	
ACADVL	NM_000018.4	
ACAT1	NM_000019.4	
ADA	NM_000022.4	
ADAMTS2	NM_014244.5	
AGA	NM_000027.4	
AGL	NM_000642.3	
AGXT	NM_000030.3	
AHI1	NM_017651.4	
AIRE	NM_000383.4	
ALDH3A2	NM_000382.3	
ALDOB	NM_000035.4	
ALG6	NM_013339.4	
ALMS1	NM_015120.4	
ALPL	NM_000478.6	
AMT	NM_000481.4	
ANO10	NM_018075.5	
ARG1	NM_000045.4	
ARSA	NM_000487.6	
ARSB	NM_000046.5	

Gene	Transcript	Technical Limitations
ARX	NM_139058.3	
ASL	NM_000048.4	
ASNS	NM_133436.3	
ASPA	NM_000049.4	
ASS1	NM_000050.4	
ATM	NM_000051.3	
ATP6V1B1	NM_001692.4	
ATP7A	NM_000052.7	
ATP7B	NM_000053.4	
BBS1	NM_024649.5	
BBS10	NM_024685.4	
BBS12	NM_152618.3	
BBS2	NM_031885.5	
BCKDHA	NM_000709.4	
BCKDHB	NM_183050.4	
BCS1L	NM_004328.5	
BLM	NM_000057.4	
BTD	NM_001370658.1	The variant NM_001370658.1:c.1270G>C (p.Asp424His) is not reported.
CAPN3	NM_000070.3	
CBS	NM_000071.3	
CC2D2A	NM_001080522.2	
CCDC88C	NM_001080414.4	
CDH23	NM_022124.6	
CEP290	NM_025114.4	
CERKL	NM_001030311.2	
CFTR	NM_000492.4	Analysis of the intron 8 polymorphic region (e.g. IVS8-5T allele) is only performed if the p.Arg117His (R117H) mutation is detected. Single exon deletion/duplication analysis is limited to deletions of previously reported exons: 1, 2, 3, 11, 19, 20, 21. CFTR variants primarily associated with CFTR-related isolated congenital bilateral absence of the vas deferens and CFTR-related pancreatitis are not included in this analysis. CFTR variants with insufficient evidence of being cystic fibrosis mutations will not be reported either.
CHM	NM_000390.4	
CHRNE	NM_000080.4	
CLCN1	NM_000083.3	

Gene	Transcript	Technical Limitations
CLN3	NM_001042432.2	
CLN5	NM_006493.4	
CLN6	NM_017882.3	
CLN8	NM_018941.4	
CLRN1	NM_174878.3	
CNGB3	NM_019098.5	
COL4A3	NM_000091.5	
COL4A4	NM_000092.5	
COL4A5	NM_000495.5; NM_033380.3	
COL7A1	NM_000094.4	
CPS1	NM_001875.5	
CPT1A	NM_001876.4	
CPT2	NM_000098.3	
CRYL1	NM_015974.3	Only whole gene deletions related to GJB2-related hearing loss are reported.
CTNS	NM_004937.3	
CTSK	NM_000396.4	
CYBA	NM_000101.4	
CYP11A1	NM_000781.3	
CYP11B1	NM_000497.4	
CYP11B2	NM_000498.3	
CYP21A2	NM_000500.9	Significant pseudogene interference and/or reciprocal exchanges between the CYP21A2 gene and its pseudogene, CYP21A1P, have been known to occur and may impact results. As such, the relevance of variants reported in this gene must be interpreted clinically in the context of the clinical findings, biochemical profile, and family history of each patient. CYP21A2 variants primarily associated with non-classic congenital adrenal hyperplasia (CAH) are not included in this analysis (PubMed: 23359698). The variants associated with non-classic disease, including but not limited to c.188A>T (p.His63Leu), c.844G>T (p.Val282Leu), c.1174G>A (p.Ala392Thr), and c.1360C>T (p.Pro454Ser) will not be reported. LR-PCR is not routinely ordered for NM_000500.9:c.955C>T (p.Gln319Ter). Individuals with c.955C>T (p.Gln319Ter) will be reported as a Possible Carrier indicating that the precise nature of the variant has not been determined by LR-PCR and that the variant may occur in the CYP21A2 wild-type gene or in the CYP21A1P pseudogene. The confirmation test is recommended if the second reproductive partner is tested positive for variants associated with classic CAH.
CYP27A1	NM_000784.4	
CYP27B1	NM_000785.4	

Gene	Transcript	Technical Limitations
DBT	NM_001918.5	
DCLRE1C	#N/A	
DHCR7	NM_001360.3	
DHDDS	NM_024887.3	
DLD	NM_000108.5	
DMD	NM_004006.2	Single exon deletion/duplication analysis is limited to exons with > 1 patient reported in the UMD database (http://www.umd.be/DMD/W_DMD/index.html), accessed Dec 29,2020 and all out-of-frame exons after exon 3. This includes deletion of exon 1, and duplication of exon 2, and del/dup for exons 3, 6~8, 11, 12, 17~22, 43~46, 48, 50~56, 58~63, 65~70, 75, 76, and 78. Single-exon detection is limited to blood samples.
DNAH5	NM_001369.3	
DNAI1	NM_012144.4	
DNAI2	NM_023036.6	
DPYD	NM_000110.4	
DYNC2H1	NM_001080463.2	
DYSF	NM_003494.4	
ELP1	NM_003640.5	
ERCC2	NM_000400.4	
ERCC6	NM_000124.4; NM_001277058.2	
ERCC8	NM_000082.4	
ETHE1	NM_014297.5	
EVC	NM_153717.3	
EVC2	NM_147127.5	
EYS	NM_001142800.2	
F11	NM_000128.4	
F9	NM_000133.4	
FAH	NM_000137.4	
FAM161A	NM_001201543.2	
FANCA	NM_000135.4	
FANCC	NM_000136.3	
FKRP	NM_024301.5	
FKTN	NM_001079802.2	
FMO3	NM_006894.6	

Gene	Transcript	Technical Limitations
FMR1	NM_002024.6	The exact size of alleles >200 CGG repeats cannot be determined; these alleles are pathogenic for X-Linked Fragile X Syndrome. Alleles with <10 repeats may fail to amplify; these alleles are benign. The repeat length for this gene may vary by +/- 1 repeat unit. Methylation is not analyzed. RP-PCR analysis of the FMR1 promoter is not routinely performed in males. Small degrees of size mosaicism, including gonadal mosaicism, may not be detected.
G6PC	NM_000151.4	
GAA	NM_000152.5	
GALC	NM_000153.4	
GALK1	NM_000154.2	
GALNS	NM_000512.5	
GALT	NM_000155.4	The D2 "Duarte" allele is not included in this analysis.
GAMT	NM_000156.6	
GBA	NM_001005741.3	The current testing method may not be able to reliably detect certain pathogenic variants in the GBA gene due to homologous recombination between the pseudogene and the functional gene.
GBE1	NM_000158.4	
GCDH	NM_000159.4	
GJB1	NM_000166.6	
GJB2	NM_004004.6	
GJB6	NM_001110219.3	Only whole gene deletions related to GJB2-related hearing loss reported.
GLA	NM_000169.2	
GLB1	NM_000404.4	
GLDC	NM_000170.3	
GLE1	NM_001003722.2	
GNE	NM_001128227.3; NM_005476.7	
GNPTAB	NM_024312.5	
GNPTG	NM_032520.5	
GNS	NM_002076.4	
GRHPR	NM_012203.2	
GRIP1	NM_021150.4	
GUSB	NM_000181.4	
HADHA	NM_000182.5	
HBA1	NM_000558.5	
HBA2	NM_000517.6	

Gene	Transcript	Technical Limitations
HBB	NM_000518.5	
HEXA	NM_000520.6	
HEXB	NM_000521.4	
HGD	NM_000187.4	
HGSNAT	NM_152419.3	
HLCS	NM_000411.8	
HMGCL	NM_000191.3	
HOGA1	NM_138413.4	
HPS1	NM_000195.5	
HPS3	NM_032383.5	
HSD17B4	NM_000414.4	
HYLS1	NM_145014.2	
IDS	NM_000202.8	
IDUA	NM_000203.5	
IL2RG	NM_000206.3	
IVD	NM_002225.5	
KCNJ11	NM_000525.4	
L1CAM	NM_000425.5	
LAMA2	NM_000426.4	
LAMA3	NM_000227.6	
LAMB3	NM_000228.3	
LAMC2	NM_005562.3	
LIPA	NM_000235.4	
LOXHD1	NM_144612.6	
LRP2	NM_004525.3	
LRPPRC	NM_133259.4	
MAN2B1	NM_000528.4	
MCCC1	NM_020166.5	
MCCC2	NM_022132.5	
MCOLN1	NM_020533.3	
MCPH1	NM_024596.5	
MED17	NM_004268.5	
MEFV	NM_000243.3	

Gene	Transcript	Technical Limitations
MESP2	NM_001039958.2	
MID1	NM_000381.4	
MLC1	NM_015166.4	
MMAA	NM_172250.3	
MMAB	NM_052845.4	
MMACHC	NM_015506.3	
MUT	NM_000255.4	
MPL	NM_005373.3	
MTHFR	NM_005957.5	As recommended by ACMG, the two common polymorphisms in the MTHFR gene - c.1286A>C (p.Glu429Ala, also known as c.1298A>C) and c.665C>T (p.Ala222Val, also known as c.677C>T) - are not reported in this test due to lack of sufficient clinical utility to merit testing (PubMed: 23288205).
MTM1	NM_000252.3	
MTTP	NM_000253.3	
MVK	NM_000431.4	
MYO7A	NM_000260.4	
NAGA	NM_000262.3	
NAGLU	NM_000263.4	
NBN	NM_002485.5	
NDUFAF5	NM_024120.5	
NDUFS4	NM_002495.4	
NDUFS6	NM_004553.6	
NEB	NM_001271208.2	
NPC1	NM_000271.5	
NPC2	NM_006432.5	
NPHS1	NM_004646.4	
NPHS2	NM_014625.4	NM_014625.3:c.686G>A(p.Arg229Gln) is not reported.
NR0B1	NM_000475.5	
NR2E3	NM_014249.2	
NTRK1	NM_002529.4	
OAT	NM_000274.4	
OCA2	NM_000275.3	
OPA3	NM_025136.4; NM_001017989.3	

Gene	Transcript	Technical Limitations
OTC	NM_000531.6	
PAH	NM_000277.3	
PC	NM_000920.4	
PCCA	NM_000282.4	
PCCB	NM_000532.5	
PCDH15	NM_033056.3	
PDHA1	NM_000284.4	
PEX1	NM_000466.3	
PEX10	NM_153818.1	
PEX12	NM_000286.3	
PEX2	NM_000318.3	
PEX26	NM_017929.6	
PEX6	NM_000287.4	
PEX7	NM_000288.4	
PFKM	NM_000289.6; NM_001166686.1	
PHGDH	NM_006623.4	
PKHD1	NM_138694.4	
PLP1	NM_000533.5	
PMM2	NM_000303.3	
POLG	NM_002693.3	
POMGNT1	NM_017739.3	
PPT1	NM_000310.4	
PRF1	NM_001083116.3	
PROP1	NM_006261.5	
PTS	NM_000317.3	
PUS1	NM_025215.6	
PYGM	NM_005609.4	
RAG1	#N/A	
RAG2	NM_000536.4	
RAPSN	NM_005055.5	
RARS2	NM_020320.5	
RMRP	NR_003051.3	
RNASEH2B	NM_024570.4	

Gene	Transcript	Technical Limitations
RPE65	NM_000329.3	
RS1	NM_000330.4	
RTEL1	NM_001283009.2	
SACS	NM_014363.6	
SCO2	NM_005138.3	
SEPSECS	NM_016955.4	
SGCA	NM_000023.4	
SGCB	NM_000232.5	
SGCD	NM_000337.6	
SGCG	NM_000231.3	
SGSH	NM_000199.5	
SLC12A6	NM_133647.1; NM_005135.2	
SLC17A5	NM_012434.5	
SLC19A3	NM_025243.4	
SLC22A5	NM_003060.4	
SLC25A13	NM_014251.3	
SLC25A20	NM_000387.6	
SLC26A2	NM_000112.4	
SLC26A4	NM_000441.2	
SLC35A3	NM_012243.3	
SLC37A4	NM_001164277.1	
SLC6A8	NM_005629.4	
SLC7A7	NM_001126106.2	
SMN1	NM_000344.3	The current testing method detects sequencing variants in exon 7 and copy number variations in exons 7-8 of the SMN1 gene (NM_022874.2). Sequencing and deletion/duplication analysis are not performed on any other region in this gene. About 5%-8% of the population have two copies of SMN1 on a single chromosome and a deletion on the other chromosome, known as a [2+0] configuration (PubMed: 20301526). The current testing method cannot directly detect carriers with a [2+0] SMN1 configuration, but can detect linkage between the silent carrier allele and certain population-specific single nucleotide changes. As a result, a negative result for carrier testing greatly reduces but does not eliminate the chance that a person is a carrier. Only abnormal results will be reported.
SMPD1	NM_000543.5	
STAR	NM_000349.3	

Gene	Transcript	Technical Limitations
SUMF1	NM_182760.4	
SURF1	NM_003172.4	
TAT	NM_000353.3	
TCIRG1	NM_006019.4	
TECPR2	NM_014844.5	
TF	NM_001063.4	
TGM1	NM_000359.3	
TH	NM_199292.3	
TMEM216	NM_001173990.3	
TPP1	NM_000391.4	
TRMU	NM_018006.5	
TTPA	NM_000370.3	
TYMP	NM_001953.5	
USH1C	NM_005709.4	
USH2A	NM_206933.4	
VPS13A	NM_033305.3	
VPS13B	NM_017890.4	
VRK1	NM_003384.3	
VSX2	NM_182894.3	
WNT10A	NM_025216.3	If detected, certain common variants which are associated with autosomal dominant selective tooth agenesis are not reported. These variants are associated with low penetrance for autosomal recessive disease and are commonly found as homozygous in healthy controls.
XPA	NM_000380.4	
XPC	NM_004628.5	
ZFYVE26	NM_015346.4	