Next-generation sequencing

Carrier Reporter Software for CarrierSeq ECS research

Example paired results report

- Using the Carrier Reporter Software for Ion Torrent™ CarrierSeq™ Expanded Carrier Screening (ECS) research, easily generate reports that are customized to the needs of your laboratory and your customers*
- Access demographics, genetic findings, and associated background information by sample
- Connect samples and generate paired result reports—combined analysis includes paired residual risk based on ethnicities, and residual risk calculations using risk data known for each gene

* Use the Carrier Reporter Software setup tool to define report criteria.

CarrierSeq™ ECS

ID	NA04394__CSeqVal_L1_T2.19_540_v1	**Sample Number**	NA04394__CSeqVal_L1_T2.19_540_v1	**Offering**	HS_Novel_NoCallActive
Sex at Birth	♂ Male				

ID	NA05117__CSeqVal_L1_T2.01_540_v2	**Sample Number**	NA05117__CSeqVal_L1_T2.01_540_v2	**Offering**	HS_Novel_NoCallActive
Sex at Birth	♀ Female				

HS_Novel_NoCallActive Results - Positive

RISK DESCRIPTION	♂	♀
Von Willebrand disease Reproductive risk: Predicted 1:4 Autosomal Recessive	**Carrier** VWF:c.4413del, Pathogenic, 12: 6019004-6019005, ENST00000261405.9, p.Asp1472ThrfsTer53	**Carrier** VWF:c.7988G>C, Conflicting interpretations, 12: 5952518-5952518, NM_000552.4, p.Arg2663Pro
Deafness, autosomal recessive 16 Reproductive risk: 1:1 Autosomal Recessive	**Affected - Homozygote** STRC:c.455_456del, Pathogenic, 15: 43617964-43617966, ENST00000450892.7, p.Gly152AlafsTer12	**Carrier** STRC:g.43599499-43610484 LOSS, Pathogenic, 15: 43599499-43610484 **Affected - Homozygote** STRC:c.455_456del, Pathogenic, 15: 43617964-43617966, ENST00000450892.7, p.Gly152AlafsTer12
Duchenne muscular dystrophy Reproductive risk: 1:2 for an affected male offspring X-Linked	**Unknown** DMD:c.831+143_831+144insCA, c.32-218C>T, c.5586+94_5586+95dup, c.5448+169A>T, c.2141+67G>A, c.4845+167C>T, c.4072-389G>T, c.3922-204C>G, c.2208-178G>A, Vous, See "VOUS List", X: 32698969-32698970, X: 33020418-33020418, X: 32345847-32345848, X: 32348237-32348237, X: 31173472-31173472, X: 32380343-32380343, X: 32412302-32412302, X: 32438594-32438594, X: 31169779-31169779, ENST00000357033.8, ENST00000343523.6 **No Call** DMD:c.2195dup, See "No Call List", X: 32518104-32518104, NM_004006.2, p.His732Glnfs	**Carrier** DMD:g.31965009-31968838 LOSS, Pathogenic, X: 31965009-31968838
Spinal Muscular Atrophy Reproductive risk: Predicted 1:4 Autosomal Recessive	**Carrier** SMN1:c.5C>G, Pathogenic, 5: 70925108-70925108, NM_000344.3, p.Ala2Gly **Risk Factor** SMN1:c.*3+80T>G, Benign, 5: 70952074-70952074, NM_423434.3	**Carrier** SMN1:g.70951920-70953012 LOSS, Pathogenic, 5: 70951920-70953012

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RISK DESCRIPTION	♂	♀
Omenn syndrome / T- B- severe combined immunodeficiency Residual risk: Reduced Autosomal Recessive	**Affected - Homozygote** RAG1:c.1178del, Pathogenic, 11: 36574477-36574478, ENST00000299440.5, p.Gly393AlafsTer10	**No findings** RAG1, No disease-causing variant detected.
Gaucher disease, type I Residual risk: Reduced Autosomal Recessive	**Affected - Compound Heterozygote** GBA:c.1171G>C, Likely Pathogenic, 1: 155236298-155236298, NM_001005741.2, p.Val391Leu **Affected - Compound Heterozygote** GBA:c.1448T>C, Pathogenic, 1: 155235252-155235252, NM_001005741.2, p.Leu483Pro	**Unknown** GBA:c.762-257C>T, c.*102T>C, c.1388+141A>G, c.1000-81A>C, c.*92G>A, c.762-180A>G, Vous, See "VOUS List", 1: 155237835-155237835, 1: 155234893-155234893, 1: 155235540-155235540, 1: 155236550-155236550, 1: 155234903-155234903, 1: 155237758-155237758, ENST00000327247.9
Lipoprotein lipase deficiency, familial Residual risk: Reduced Autosomal Recessive	**No findings** LPL, No disease-causing variant detected.	**Carrier** LPL:c.953A>G, Pathogenic, 8: 19956018-19956018, NM_000237.3, p.Asn318Ser
Xeroderma pigmentosum, group C Residual risk: Reduced Autosomal Recessive	**Carrier** XPC:c.1001C>A, Pathogenic, 3: 14158882-14158882, NM_004628.4, p.Pro334His	**Unknown** XPC:c.901-70A>C, c.2605-51A>G, Vous, See "VOUS List", 3: 14159900-14159900, 3: 14146210-14146210, ENST00000285021.11
Phenylalanine hydroxylase deficiency (including phenylketonuria) Residual risk: Reduced Autosomal Recessive	**Unknown** PAH:c.442-309A>G, c.352+164T>A, c.1200-186T>C, c.442-223C>T, g.102917446A>G, c.442-193A>G, c.913-341A>G, c.843-268T>C, c.842+201G>T, Vous, See "VOUS List", 12: 102866972-102866972, 12: 102894571-102894571, 12: 102840701-102840701, 12: 102866886-102866886, 12: 102917446-102917446, 12: 102866856-102866856, 12: 102847292-102847292, 12: 102852024-102852024, 12: 102852614-102852614, ENST00000553106.6, 12	**Carrier** PAH:c.60+62C>T, Likely Pathogenic, 12: 102917009-102917009, NM_000277.2
Albinism, oculocutaneous, type IA Residual risk: Reduced Autosomal Recessive	**No findings** TYR, No disease-causing variant detected.	**Carrier** TYR:c.1205G>A, Conflicting interpretations, 11: 89284793-89284793, NM_000372.4, p.Arg402Gln
Triple A syndrome Residual risk: Reduced Autosomal Recessive	**Unknown** AAAS:c.1088-59A>G, Vous, See "VOUS List", 12: 53308587-53308587, ENST00000209873.9	**Carrier** AAAS:c.1066_1067delCT, Pathogenic, 12: 53308744-53308746, NM_015665.5, p.Leu356Valfs

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RISK DESCRIPTION	♂	♀
Alport syndrome, autosomal recessive Residual risk: Reduced Autosomal Recessive	**Unknown** COL4A4:c.594+96C>T, c.871-60_871-38del, c.558+118C>A, c.1029+72G>A, c.735+104C>T, c.4522+72G>A, c.490-121T>G, c.2716+187C>T, Vous, See "VOUS List", 2: 227111582-227111582, 2: 227102907-227102930, 2: 227114510-227114510, 2: 227101432-227101432, 2: 227108477-227108477, 2: 227010241-227010241, 2: 227114817-227114817, 2: 227055758-227055758, ENST00000396625.4 **No Call** COL4A4:c.2092G>A, See "No Call List", 2: 227060208-227060208, NM_000092.4, p.Gly698Arg	**Carrier** COL4A4:c.4932delCinsTT, Likely Pathogenic, 2: 227007466-227007466, NM_000092.4, p.Ala1645Cysfs

NO FINDINGS FOR THE REMAINING GENES TESTED

The paired risk reflects the risk of having a child that is affected by the genetic disease.

Residual risk represents the post-test likelihood of carrier status and the paired residual risk represents the likelihood of disease inheritance by offspring of a pair. Residual and paired residual risk predictions are standard carrier screening calculations, these estimates can vary by ethnicity and apply to negative family histories and negative test results. Note that inaccurate ethnicity information can result in risk calculation errors.

Paired residual risk represents the likelihood of disease inheritance by offspring of a pair, including when one member of a pair was found to be a carrier of a variant in a gene, while the other tested negative for this gene. There is a very low risk that following a negative test result, this member of a pair will be a carrier of a rare or previously uncharacterized genetic change that was not targeted by the assay.

SMN1 - Risk Factor

This expanded preconception screening tests in addition the g.27134T>G variant which was suggested to be associated with a silent carrier state of the SMN1 gene (two copies of the gene on one allele and zero copies of the gene on the other allele, i.e., cis configuration). It is important to emphasize that the test estimates but cannot confirm the exact number of SMN1 copies carried by the tested individual. The presence of the variant is reported only if the test estimates that the tested individual carries two copies of the SMN1 gene. A finding of this variant combined with two copies of the SMN1 gene may indicate an increased chance of a silent carrier state but cannot confirm it (Luo M, et al. 2014). This variant is not reported if the test estimates that the tested individual carries more than two copies of the SMN1 gene.

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Disease Description

Xeroderma pigmentosum, group C

A severe autosomal recessive condition characterized by an extreme sensitivity to ultraviolet (UV) rays from sunlight. This condition mostly affects the eyes and areas of skin exposed to the sun.People with xeroderma pigmentosum have a greatly increased risk of developing skin cancer. The median age at death in persons with XP is 37 years.

Triple A syndrome

Triple A syndrome, also known as Allgrove syndrome, is an autosomal recessive disorder of the nervous system with variable severity and age at onset. Signs and symptoms usually include alacrima, Addison disease or adrenal insufficiency, and achalasia, and may include peripheral neuropathy, muscle weakness, movement disorders, intellectual disability, optic atrophy, hyperkeratosis of the palms and soles of the feet, other skin abnormalities, and dysautonomic problems. Treatments may include surgical and medical therapies, and focus on management of symptoms. (Brooks, PMID:16098009).

Duchenne muscular dystrophy

Duchenne Muscular Dystrophy is a X-linked recessive disorder that affects skeletal and heart muscles. Skeletal muscle loss causes major weakness that affects movement. Symptoms appear in early childhood and rapidly worsen. Most males affected with DMD die before thirty years of age due to heart or respiratory failure.

Spinal Muscular Atrophy

Spinal muscular atrophy is an autosomal recessive disorder, that manifests in various degrees of severity, which all have in common progressive muscle wasting and mobility impairment. Proximal muscles and lung muscles are affected first. Other body systems may be affected as well, particularly in early-onset forms of the disorder.

Alport syndrome, autosomal recessive

Alport syndrome, COL4A4-related, is an autosomal recessive disorder characterized by hearing and vision loss and impaired kidney function resulting in high levels of protein in their urine. The symptoms may be more common among men.

Von Willebrand disease

Von Willebrand disease

Gaucher disease, type I

Gaucher disease is an autosomal recessive disorder, which occurs when a type of large fatty material accumulates to excessive levels in multiple organs and tissues. The liver, spleen, lungs and bone marrow are the most commonly affected organs. Symptoms include an enlarged liver and spleen, a reduced number of red blood cells and platelets, bone abnormalities, and rarely, lung impairment.

Omenn syndrome / T- B- severe combined immunodeficiency

Omenn syndrome (OS) is an autosomal recessive inflammatory condition characterized by no immune protection from bacteria, viruses, and fungi. Affected Individuals prone to repeated and persistent infections that can be life-threatening..If not treated in a way that restores immune function, children with Omenn syndrome usually survive only until age 1.

Lipoprotein lipase deficiency, familial

Familial lipoprotein lipase deficiency is an autosomal recessive disorder with variable severity and age at onset. Symptoms typically manifest before age 10, with some individuals showing symptoms by age 1. Signs and symptoms may include severe hypertriglyceridemia with episodes of abdominal pain due to pancreatitis, acute pancreatitis, cutaneous xanthomas, hepatosplenomegaly, neurological problems. Some carriers may have an increased risk of heart disease or diabetes. Treatment is dietary and may resolve symptoms. (Burnet, PMID: 20301485).

Albinism, oculocutaneous, type IA

Albinism, oculocutaneous, type IA is an autosomal recessive disorder. Affected individuals typically have very fair skin and white or light-colored hair. Albinism also reduces pigmentation of the colored part of the eye. They usually have vision problems. Long-term sun exposure greatly increases the risk of skin damage and skin cancers.

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Deafness, autosomal recessive 16

Nonsyndromic hearing loss is an autosomal recessive disorder. It is a partial or total loss of hearing that is not associated with other signs and symptoms.

Phenylalanine hydroxylase deficiency (including phenylketonuria)

Phenylalanine hydroxylase deficiency is an autosomal recessive disorder, that is characterized by increased levels of phenylalanine in the blood. If untreated, individuals can develop symptoms including intellectual disability, seizures, behavioral problems, psychiatric disorders and musty or mouse-like odor.

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No Call List

NA04394__CSeqVal_L1_T2.19_540_v1 **(60 Genes 158 Variants)**
PYGM c.1797delT **TCIRG1** c.480dup **NAGLU** c.4G>T, c.142T>C, c.82delG, c.144C>A, c.1A>G, c.2T>C **SMPD1** c.1101dup
DBT c.1282-5_1282-2delTCTA **CEP290** c.289G>T, c.268A>T, c.3175delA, c.2390delA, c.3175dupA, c.3176delT
EMD c.359_362del, c.284_298delATGAAGAGAGCTACT, c.266-2A>G, c.135dup, c.325G>T, c.121_155del35, c.110_112del, c.130C>T, c.314_315del, c.116_143del, c.355C>T, c.153del, c.315T>G, c.103G>T, c.123C>G, c.123C>A, c.153dupC
BBS4 c.77-220delA **EYS** c.1211delA, c.1211dup, c.863-4dup **RARS2** c.1054_1055del **G6PD** c.1478G>A, c.1387C>T **ALG6** c.634dup
ABCC8 c.2695-1G>C, c.2702T>C, c.2752C>T, c.2784G>A, c.2767C>T, c.2800C>T, c.2698-2A>G, c.2698-2A>T, c.2783G>A
GAA c.169C>T, c.172C>T, c.236_246delCCACACAGTGC, c.258del, c.258dupC
BCKDHB c.937del, c.951+1G>T, c.841-1G>C, c.885del, c.902T>G, c.853C>T, c.853delC **GP1BA** c.1480del
HBA2 Hb^{G-Philadelphia}, c.179G>A, c.142G>C, c.178G>C, c.186G>C, c.207C>A **RPGRIP1L** c.1421delA
F8 c.5960_5964delAAGAG, c.5960_5961del, c.5961delA **BBS10** c.235dup **PCCA** c.923dupT **CYP21A2** c.923dup
COL4A4 c.2110G>A, c.4932delCinsTT, c.2084G>A, c.2092G>A, c.2100_2102delTGGinsGTGT **DOK7** c.55-1G>T, c.1138dupG
ATP6V1B1 c.1148_1149insC **BLM** c.3210+2delT, c.3210+3A>T **SLC26A2** c.438dup, c.438delT **LAMA2** c.5072-5154del
IDUA c.60_61delGCinsA, c.64C>T, c.-2C>G, c.53T>C, c.965T>A, c.972+1G>A, c.1A>C, c.46_57delTCGCTCCTGGCC, c.3G>A, c.65del, c.972+2T>C
DNAH5 c.5563dupA **ABCB4** c.100dup **PCDH15** c.1101del **TYMP** c.1231_1243del
MTM1 c.961_962del, c.1036T>C, c.1014_1015insT, c.969dup, c.969del, c.958T>C, c.1040T>G, c.949dup, c.1053+1G>C, c.1053+1G>A
CYP27B1 c.171dup **BRIP1** c.1935+11_1935+13delGTT **TPO** c.2421del **CBS** c.833T>C **NPHP1** g.110168528del, c.555dupA
SLC17A5 c.349dupT **CDH23** c.4877A>C **ASL** c.889C>T, c.918+5G>A
DMD c.3580C>T, c.2195dup, c.3603+1G>T, c.3535G>T, c.3532G>T, c.3603+2dup, c.3603+3A>T, c.3603+2T>A, c.3603+2T>G
LDLR c.1733T>C **FKTN** c.1167dupA **FKRP** c.-272G>A, c.142delC **ATP8B1** c.614dup **AGL** c.4221delA, c.4221dupA
FANCA c.549G>A, c.548G>A **MCOLN1** c.32-2A>G, c.38_41dup **RPE65** c.1067dup, c.1067delA **GALC** c.1162-4delT
GNPTG c.15_23dup, c.29T>A, c.53-2A>G **STRC** c.4561dup **PPT1** c.169dupA **MAN2B1** c.1A>G **ERCC5** c.205C>T, c.215C>A
ERCC6 c.1518delG **NAGS** c.1307dup **VSX2** c.71_72insG

NA05117__CSeqVal_L1_T2.01_540_v2 **(49 Genes 97 Variants)**
MECP2 c.1244dup **NAGLU** c.82delG, c.144C>A, c.2T>C, c.142T>C, c.1A>G, c.4G>T **SGCA** c.168delC **GNPTAB** c.10A>C
NBN c.1780del **MMUT** c.1022dup **CEP290** c.2390delA **ACADS** c.1A>G, c.29_35dup, c.32delG **TMC1** c.15dupA
GP1BB c.340C>T, c.338A>G
ABCC8 c.2784G>A, c.2698-2A>G, c.2698-2A>T, c.2783G>A, c.2800C>T, c.2702T>C, c.2695-1G>C, c.2752C>T, c.2767C>T
VPS13B c.9406-1G>T, c.9406-1G>C, c.9406-1G>A
HBA2 c.179G>A, c.207C>A, c.142G>C, c.178G>C, Hb^{G-Philadelphia}, c.98T>G, c.186G>C **MYO7A** c.19-1G>A
HBA1 c.179G>A, c.207C>G, c.187_189delGTG, c.187delG, c.134C>T, Hb^{G-Philadelphia}
BBS10 c.1856_1865delAAAAATGCCA **PCCA** c.923dupT **COL4A4** c.4820del **DOK7** c.55-1G>T **COL4A3** c.1927+2T>C, c.1927G>A
SLC26A2 c.1441delA **CANT1** c.-286+1G>A **IDUA** c.898G>A, c.876delC, c.65del, c.878_889dup **COL11A2** c.2754del
PCDH15 c.3441dupA **WAS** c.470_471del, c.466_469delAGAC, c.505+2T>G **TTN** c.59765dupC, c.56984delC
TYMP c.1226dup, c.1231_1243del, c.1219G>A **CYP27B1** c.171dup **BRIP1** c.1935+11_1935+13delGTT
CBS c.1265C>T, c.1280C>T, c.1224-2A>C **NPHP1** c.555dupA, g.110168528del **DMD** c.2169-3_2169-1delinsAA
ASL c.918+5G>A, c.889C>T **LDLR** c.1733T>C **FKTN** c.1167dupA **SLC12A3** c.1126delC **AGL** c.4221delA, c.4221dupA
F11 c.1362_1375del14 **FANCA** c.549G>A, c.548G>A **NEB** c.22378-1G>A **RPE65** c.1067delA, c.1067dup **GALC** c.1162-4delT
GNPTG c.15_23dup, c.53-2A>G, c.29T>A **NPHS1** c.3250delG, c.3250dupG **STRC** c.4561dup **ALMS1** c.60_61insTAGGAG
MAN2B1 c.1A>G **ERCC6** c.1518delG

CarrierSeq™ ECS

Variants of Unknown Significance List

NA04394__CSeqVal_L1_T2.19_540_v1 (258 Genes 909 Variants)
SMARCAL1 c.1096+28C>A **MTRR** c.1557+54T>C, c.780+168G>A, c.1557+227C>T, c.284-64C>G, c.1557+95G>A
GLDC c.635+33T>C, c.1850+87T>A, c.334+67G>C, c.1261+72G>A **GORAB** c.14C>T, c.957C>T, c.136+97del
MLC1 c.771+118G>A, c.525+153G>A **AQP2** c.607-59C>A, c.607-92A>G
ABCA12 c.1061+193_1061+196delinsCTTC, c.7680+78T>G, c.2684-138G>C, c.1657+72A>G, c.5940-156G>A, c.6648-129delinsAATGC, c.6648-126_6648-125insTC, c.5940-168T>C, c.2472+137A>G, c.4383-70G>T, c.2472+90C>A, c.5129-68T>C, c.4741-70T>A, c.3295-142A>C, c.2684-113G>C, c.694-48_694-47inv, c.2332+65_2332+68del, c.6118-78A>G, c.163+89T>A
LIPA c.230-79C>T **TSEN54** c.369+93del, c.369+109A>G **GLE1** c.322-35_322-29del
ZFYVE26 c.6986+127G>A, c.4975-75C>T, c.195-67T>G, c.1640-177T>G **AP1S1** c.430-90C>T, c.430-186C>T **MPV17** c.461+40C>T
MMUT c.1083+57C>T **SLC12A6** c.2650-39C>T
EYS c.2260-53T>C, c.6834+61T>G, c.2846+53_2846+54insTAAT, c.2039T>C, c.1599+96A>C, c.1459+20T>A, c.6078+68A>G, c.1767-74G>A
GAMT c.79T>C **MCCC2** g.71587309A>G, c.1575-64A>G **CPT1A** c.693+35_693+37delinsAGCG
ALG6 c.494+74A>G, c.346+87_346+90del **MCCC1** c.1978-57G>T, c.1978-86A>C **MYO7A** c.2904+43G>A, c.*38G>A **UPB1** c.105-6A>G
CYP27A1 c.1184+55A>C
POR c.1067-97C>T, c.1399-34_1399-33delinsCT, c.238-95G>T, c.831-68C>G, c.366+89C>T, c.831-55G>A, c.642-72G>A, c.1067-66T>C, c.1399-173G>A
TFR2 c.1996-111_1996-110insCA **BTK** c.1350-176C>T, c.1631+71C>T **HPD** c.831+53A>G, c.414+63C>T
ALDH7A1 c.246+37_246+42del
CFTR c.1767-136T>C, c.1210-13_1210-12del, c.2909-92G>A, c.1680-124T>C, c.*55_*85dup, c.3140-92T>C, c.1210-13_1210-11del, c.3469-65C>A, c.2619+86_2619+87del, c.3368-140A>C, c.4137-139G>A, c.1766+152T>A
MMADHC c.696+83G>A, c.372+54_372+55dup, c.-78G>C **GCDH** c.-86A>G, c.128-82T>G **CERKL** c.1444-148G>C
SLC45A2 c.888+62_888+64del **RTEL1** c.-93C>T, c.369-104G>A, c.467-83C>T, c.1210-181C>T
AIRE c.308-123T>C, c.538+51G>T, c.1504-67T>C
PCDH15 c.705+93C>T, c.3501+230G>C, c.1998-45A>G, c.3501+207_3501+209delinsAAT, c.1306-4362C>A, c.877-119T>A, c.594+232A>G, c.3984-82A>G, c.3122+186G>A, c.706-98G>A, c.3806+143C>T, c.2092-148T>A, c.1099-319T>A, c.3233-147del, c.1306-203T>C, c.4368-275del, c.475-299G>A, c.1099-282G>T, c.985+227A>G, c.2220+298T>C, c.1305+268A>C, c.2092-168C>T, c.1784+91C>T, c.986-208_986-205del, c.4211+73_4211+81dup, c.3983+140_3983+141insCAA, c.3806+90del, c.1785-51T>G, c.2527-177C>G, c.4367+1986del, c.2527-246_2527-245dup, c.4374-781C>T, c.1997+244C>T, c.157+75G>A, c.2091+212C>T, c.2092-154_2092-148delinsCTTTTTA
XPC c.104-88A>G, c.2421-76T>C, c.2028C>T, c.412+34G>A **AAAS** c.1088-59A>G **PLA2G6** c.894+47G>A, c.2277-67T>C
GNS c.21C>G, c.253-116G>A
PKHD1 c.11506+76G>A, c.5909-22C>A, c.8107+81T>A, c.7733+61_7733+63delinsTTT, c.7733+63C>T, c.8108-64G>A, c.11506+104G>A, c.7215+102T>A
GHRHR c.*147A>C, c.57+79C>T **HLCS** c.1179+53A>G, c.1520-124G>A, c.1796-66T>G **TTPA** c.664-63G>T
ASL c.978+63C>T, c.12+105C>T **BBS2** c.613-54C>G **BBS1** c.518+55C>T
ABCA4 c.4352+54A>G, c.5196+1078del, c.5585-120G>A, c.5460+62G>A **EIF2AK3** c.1306+28A>C **ACADSB** c.1229-84C>T
RPE65 c.11+99T>A **SLC6A8** c.395-96T>C **STAR** c.65-59del **TH** c.1200+83A>T, c.488-44C>T
STRC c.4546-69C>T, c.4376-34_4376-33delinsAT, c.4219-96G>T, c.2783+124G>A, c.3498+401G>A, c.3307-43_3307-42insGACACACACACA, c.2481-322G>A
PAH c.442-193A>G, c.352+164T>A, g.102917446A>G, c.1200-186T>C, c.842+201G>T, c.442-309A>G, c.442-223C>T, c.913-341A>G, c.843-268T>C
NDUFAF5 c.717+80A>G **MKS1** c.1436G>A **PPT1** c.433+79A>G
ATM c.6198+116T>C, c.5006-170G>A, c.5006-68T>G, c.-30-79A>G, c.8671+104T>C, c.8787-315T>C, c.2250+221T>C, c.2467-123T>A, c.-30-44T>C, c.6007-125T>G, c.7927+142G>A, c.5918+123T>C, c.1066-294A>G, c.2638+176G>C, c.8850+60A>G, c.*44A>G, c.3993+197G>A, c.8786+90G>A, c.4611+213A>G, c.496+221C>T
TECPR2 c.*60A>G
CC2D1A c.196+163G>A, c.1940+61C>T, c.2454+33C>T, c.379-271T>C, c.1642-8C>T, c.61-63T>C, c.*115C>T, c.1357-251C>G
TRMU c.1019-83G>C, c.874-55C>T, c.82+130T>C **GFM1** c.1140+82T>C, c.1140+57C>T, c.747-87A>G
PIGN c.2619+46G>T, c.964-84T>A, c.674+163C>G, c.2370+186T>A, c.443-68T>C **GBE1** c.2052+51_2052+52insCTT
HEXA c.346+13C>T, c.-226A>G, c.987-177C>T **CHM** c.315-1541C>A **PYGM** c.528+51C>T, c.529-82G>A, c.528+74C>A
IKBKAP c.3856-82_3856-81delinsCT, c.1643+145G>A, c.3347-90A>G, c.741-92_741-89dup, c.552+42_552+43dup

CarrierSeq™ ECS

PEPD c.1344+44_1344+47delinsGCCA
LYST c.5461-58T>G, c.10375-159A>C, c.10940+91G>T, c.4689-166T>C, c.10701+111dup, c.3394-90T>C, c.4689-149C>T, c.10375-196T>A, c.9106+58A>G, c.10701+41G>A
MED17 c.1329-71_1329-69delinsGAT **BBS9** c.531C>A, c.1330-62C>T, g.33635227-33635228, c.1963-53A>G
ACADM c.118+133A>G, c.486+71G>A **LDLRAP1** c.532+138_532+139del, c.617-102A>G **ACADS** c.934-74C>T **CTSD** c.827+111del
CTSC c.318+53C>A, c.318+101A>T, c.173-79A>T
BBS4 c.1036+114G>A, c.1248+68G>A, c.643-102T>C, c.332+150G>A, c.1439C>T, g.72686093T>C **GP1BB** c.*107C>T
ARG1 c.826+76dup **GAA** c.2800-169C>T **ACAD9** c.1564-55A>G, c.1359-63T>C **F2** c.1726-59G>A
DDB2 c.603-135C>T, c.1235-79T>C, c.456+65A>G **HADHA** c.1393-62A>C **F8** c.1752+134C>T, c.2947G>A **F9** c.253-82G>T
SLC7A7 c.1430-74G>A, c.1246-73A>C, c.1430-55T>C **CYP21A2** c.*52C>T **IVD** c.154-116C>T, c.154-131_154-130del
AGPS c.442-64C>T, c.1545+77T>A **DPYD** c.1524+176G>T, c.2908-69A>G, c.2908-58G>C, c.680+139G>A, c.1740+39_1740+40inv
ALDOB c.800-76T>C, c.999+84T>C, c.999+105G>A **MOCS1** c.-44G>A, c.757+61T>G **CRB1** c.653-9553T>G, c.3413+212T>C, c.653-53T>G
FH c.1108+98C>A **OAT** c.200-182C>T **IDUA** c.1728-87C>A, c.1727+72T>G, c.493+132G>C
COL11A2 c.4812+151G>A, c.3757-82_3757-81inv, c.3702+151C>T, c.861+981A>G, c.4135-119A>G
GBA c.115+174_115+175del, c.1000-81A>C, c.762-180A>G, c.1388+141A>G, c.*92G>A, c.762-257C>T **WAS** c.505+30A>G
HSD17B4 c.*6A>G, c.2197-84G>A **ABCB11** c.2343+127T>C, c.1638+80C>T
WRN c.1982-156T>C, c.839+56C>T, c.210-90G>A, c.355+91C>T, c.356-85C>T, c.2826-191C>T, c.2732+64A>G, c.3983-95C>T, c.2089-3168C>T
CHRNG c.921-56C>G, c.806-69G>A, c.195+19G>A, c.921-68del, c.1092G>A, c.1035+64C>T
DMD c.4845+167C>T, c.4072-389G>T, c.5448+169A>T, c.3922-204C>G, c.2141+67G>A, c.831+143_831+144insCA, c.5586+94_5586+95dup, c.32-218C>T, c.2208-178G>A
LDLR c.1201+57G>A, c.2044-53G>A, c.1885+24_1885+33del **EVC2** c.2262-183A>G, c.467-57T>C, c.2373C>T, c.3032+83A>G
GCH1 c.453+53C>T, c.626+37T>C **GPR56** c.1665-99G>A, c.1167+77C>A, c.*74C>A **AGL** c.665-73A>G, c.3836+53T>A, c.4260-97G>A
F11 c.56-85T>C, c.453C>T **PEX10** c.600+38G>A **FAH** c.*38_*42delinsCTTTG **LRPPRC** c.3275+97T>C, c.888C>T
ALMS1 c.647-57G>A, c.1574_1576del, c.69_74del, c.647-80A>G **OTC** c.540+134G>A, c.540+156del **DCLRE1C** c.-96+176G>A
MRE11 c.545-44C>T, c.659+30C>G, c.403-107G>A, c.846-60T>A **AMHR2** c.1425+77A>G, c.*68T>C **NAGLU** c.532-96A>G
SACS c.12437delinsT, c.2093+55C>T **CAPN3** c.445-57_445-54del, c.445-49_445-45del, c.633-69G>A, c.121-105G>C
SLC39A4 c.1074+60G>A, c.398T>C **LHCGR** c.234-65A>T **HGD** c.711C>A **CYBB** c.484-1068T>C, c.804+118A>G
LIFR c.2335+39A>G, c.398-56A>G **OCRL** c.723-60A>C **RPGRIP1L** c.1104-82C>T **MAT1A** c.951+98T>C, c.769-195T>A
EDAR c.655+30T>C **ALDH3A2** c.472-150G>C
PREPL c.220-142C>A, c.220-129A>G, c.1896+168G>A, c.969+259C>T, c.1156-160G>A, c.616+108G>A, c.1746+117C>T, c.616+80G>T, c.752+82C>T, c.1896+111T>C, c.220-95C>T, c.752+228A>T, c.410-128_410-126del, c.*1259C>G
COL4A4 c.735+104C>T, c.594+96C>T, c.4522+72G>A, c.558+118C>A, c.1029+72G>A, c.490-121T>G, c.2716+187C>T, c.871-60_871-38del
DOK7 c.*105T>C, c.*55C>G, c.1261+82C>T **COL4A3** c.324+73C>T, c.828+59C>G, c.468+72T>C **BLM** c.3358+169A>C, c.3559-95G>A
NDRG1 c.327-67G>A, c.891+61G>A **ACAT1** c.941-75A>C, c.827-158T>A **LOXHD1** c.4148C>T, c.416-107A>G
TPO c.2652C>T, c.*34A>T, c.2386+59C>T, c.2006+90C>A, c.2006+39A>G **NLRP7** c.2726+30_2726+33del, c.2726+98C>T
PSAP c.1005+44C>T, c.1432-147G>A, c.16C>T, c.175-62del
NPHP1 c.1521-116C>T, c.329+76C>T, c.940-118C>T, c.1327-61C>T, c.1810+148G>A, c.*31C>T
CDH23 c.5125C>T, c.1858+79A>G, c.625-138G>A, c.4209+99G>A, c.3369+58C>T, c.9319+72_9319+73insTC, c.2751C>G, c.6254-79A>T, c.4489-27T>G, c.4360-94C>T, c.1134+13A>G, c.5188-128T>A, c.4617+54C>T
SMN1 c.627+92T>C, c.273+113C>A, c.627+160T>A, c.81+158A>C, c.274-65G>A, c.82-316G>A, c.*211_*212del
EIF2B5 c.765+61G>A, c.1303-36C>T **PDHA1** c.946-60C>T **ATP8B1** c.1220+59C>T, c.555-167A>G **HPS1** c.1398-130T>C
HPS4 c.706+36G>A
FANCA c.827-164G>A, c.3349-158G>A, c.596+143T>G, c.1006+182C>G, c.3513+57G>A, c.3626+158G>A, c.284-168A>G, c.522+152C>G, c.*384A>T, c.3626+216T>C, c.2505-10_2505-9del, c.1900+121G>C, c.3066+236C>G, c.3626+171A>G, c.1225+151T>C, c.*245A>G, c.3066+281C>T, c.596+74G>A, c.3627-203T>C, c.1471-73G>A, c.2223-83G>A, c.3066+343G>A, c.1827-151A>C
SLC4A11 c.777+140C>A, c.2606+51A>G, c.1463+97T>G, c.778-31_778-26delinsCCACAGGGGTGGTGGA
ASNS c.488-80T>C, c.1477-32G>A, c.1238+52A>G, c.-23-44T>C **HPS3** c.1400+97A>G, c.1692-192T>G, c.2107-57A>G
FANCC c.897-221C>A, c.687-288C>T, c.897-234A>G, c.1330-141T>C, c.997-216_997-215insATTATTT

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NEB c.2416-6G>T, c.1470+177G>A, c.18997-196A>G, c.21102+280C>G, c.22905+66T>C, c.24301-286T>C, c.3879+337C>G, c.23649+282C>G, c.17014-134T>C, c.13789-122C>T, c.23836-55C>G, c.13993-32A>G, c.15450+194G>A, c.20368-57G>A, c.20049+337A>G, c.613-160T>G, c.8890-140C>T, c.1570-146A>T, c.12747+115G>C, c.21418-296T>C, c.6184-136_6184-135del, c.15237A>G, c.10452+107G>A, c.23241+303G>A, c.8161-118A>T, c.402+101A>G, c.22590+237G>A, c.22591-126A>G, c.5452-177C>G, c.21523-147A>G, c.4719+350C>T, c.4507-105A>T, c.9724-133T>G, c.17844+65T>C, c.2835+215G>A, c.6076-149A>G, c.2415+228A>G, c.10452+202C>T, c.10872+55G>A, c.12331-122C>T, c.8160+84G>A, c.11290-91G>A, c.24580-81A>G, c.78+106T>G, c.19429-193T>C, c.294+52T>G, c.23016+23T>C, c.6702+150C>T, c.18471+201C>T, c.19731+103G>T, c.17430+57G>C, c.4611+70T>C, c.15451-32A>G, c.21103-77T>A, c.23242-50_23242-47dup, c.18997-173G>A, c.21840+82A>G, c.6076-88_6076-87del, c.8374-207A>G, c.19836+213G>C, c.6702+68T>C, c.19207-99dup, c.2638-253A>T, c.613-121T>C, c.24114+263_24114+266dup, c.1675-67C>T, c.15247-122C>T, c.17510A>G, c.20466+148T>C
ACSF3 c.1239+57G>C, c.977+119A>G, c.667-101T>C, c.978-83C>G, c.667-77G>C, c.977+185T>C **GRHPR** c.509G>A, c.494-68A>G
SEPSECS c.1026+89C>T, c.389-52A>G **GH1** c.456+90T>A
CPS1 c.3142-119G>C, c.127-93T>A, c.15_16insTTC, c.2568+201A>G, c.4101+62A>G, c.127-98G>T, c.3337-79C>T
CYP11B2 c.799+17G>A, c.1201-12C>T, c.596-41_596-39delinsTCC, c.1122-10C>T, c.955-115_955-113delinsCG
CYP11B1 c.955-39C>G, c.1122-80T>G, c.799+119T>G, c.1122-197A>G, c.1122-109G>C, c.800-75T>G
ALPL c.862+58C>T, c.792+76T>C, c.182-15C>G **TPP1** c.1426-78T>C **DHCR7** c.831+69G>A **SLC26A4** c.2090-52_2090-49dup
SLC26A3 c.*113T>C **DNAL1** c.42+50T>C **GALK1** c.794-126T>C, c.611+56del **CIITA** c.52+64T>C, c.3150-118A>G
ACADVL c.412-169C>A, c.412-89T>C, c.412-92_412-76del **EDA** c.397-96293T>C
ITGB3 c.1914-139_1914-138insTG, c.2015-85T>C, c.1914-267G>T, c.2015-201A>G **TAT** c.408+58A>C, c.1042-72G>T
DYSF c.343-42G>T, c.1512A>T, c.1397+49G>A, c.938-20del **ETFA** c.736-77_736-76insTAAGG **LAMC2** c.269-64C>T, c.2457-115C>T
TCIRG1 c.808-52C>T **NR2E3** c.119-28_119-13del **SGSH** c.507-129G>A, c.250-72G>A
ADAMTS2 c.1133-57C>T, c.1122C>T, c.2618-54C>T **SGCD** c.712_714del **CNGA3** c.790T>A **SLC37A4** g.119026552-119026552
ATP7A c.1543+86dup **ABCD1** c.1635-125C>T **CEP290** c.853-127_853-125dup, c.6645+67G>A
POLG c.2734+39_2734+40insGTAG, c.3643+79T>C **BCKDHA** c.853+61T>C, c.995+90C>T **TSFM** c.57+47C>T
MKKS c.1161+58A>G, c.1272+194G>A **DNAI2** c.1722+78G>A, c.1495-152C>A, c.747C>T **UGT1A1** c.-40_-39insTA, g.233758936A>C
VWF c.7549-59A>C, c.220+52T>C, c.2282-122_2282-121inv, c.5665-118G>A, c.1110-73T>A, c.2282-133T>C, c.5664+128G>T, c.5843-111A>G, c.5664+106T>C
ABCC8 c.4611+54G>C, c.2295-36_2295-34delinsTTC **BCKDHB** c.952-151G>A, c.197-46del
ABCC6 c.1431+73C>G, c.2787+62T>C, c.1780-86G>T, c.2995+142C>T, c.346-38A>G, c.1867+60A>G
VPS13A c.283+269T>C, c.8667+307A>G, c.9077+55G>C, c.9474+152C>T, c.5416-132A>G, c.8667+372C>T, c.*222G>T, c.*184A>G, c.8035+371G>T, c.1161+134G>A, c.2288+210A>C, c.9275+139G>C, c.188-88_188-87insT, c.754+273A>G, c.9190-54T>G, c.7027-54A>G, c.616-83C>T, c.3813-151A>T, c.101-296C>T, c.2428-181A>G, c.101-62A>G, c.2512+116A>G, c.1596-74T>C, c.4412+215C>A, c.144+236T>C, c.8016G>C, c.101-7T>C, c.4957-52G>A, c.2171-174C>T
VPS13B c.11495+19G>A, c.1844-51G>A, c.2824+97G>C, c.10388A>G **PEX2** c.-17-41G>T **POMGNT1** c.1212-66T>C, c.1212-81C>T
HAX1 c.317-33C>T **EVC** c.939+63C>A, c.940-91G>A, c.617+133G>C, c.617+154A>G, c.940-71G>A **PCCA** c.184-17_184-16del
NPC1 c.1947+90T>C, c.2605-70A>G **ACOX1** c.775-217C>T **NDUFS6** c.187-53_187-50del **PEX6** c.1368-177G>A, c.1479+110C>T
NDUFS4 c.351-101G>A **CNGB3** c.852+55C>T, c.643+135A>T, c.339-139G>A, c.643+126_643+129del
AGXT c.777-44A>G, c.595+100G>A **ASPA** c.*3A>G **ATP6V1B1** c.-9del, c.274-72A>C **CANT1** c.-342+53A>G
LAMA2 c.5727-24_5727-21delinsACTG
DNAH5 c.4797-93C>A, c.2744-55_2744-42delinsCATCCATCCG, c.6249+98_6249+127del, c.277+118A>G, c.8010+79_8010+80del, c.9721-63T>A, c.6444+8_6444+11delinsGTCT, c.12499+184G>A, c.12500-194T>G, c.6250-120C>T, c.5710-58G>A
LAMA3 c.2502+189T>C **TYRP1** c.1554G>C, c.709-88T>C **ETFDH** c.465+73G>A, c.832-104A>C
SLC3A1 c.766-200G>A, c.765+155G>A, c.1137-334C>T, c.1137-358G>A
SAMHD1 c.626-256T>C, c.1271-59A>G, c.510-74T>G, c.1503+114_1503+115insAAGAAGTCATC, c.276-310G>T
TTN c.8764+14_8764+15del, c.13859-6757G>A, c.10742-112A>T, c.26963-24A>G, c.9025+56A>G, c.9025+102C>A, c.20954-112_20954-109del, c.7978+56G>A
CBS c.-8-159C>T, c.954+127G>A **VPS53** c.2328+45dup **DNAI1** c.297A>G, c.978A>C **NTRK1** c.428+68T>C, c.2121C>T, c.2188-108C>T
SLC12A3 c.2447-72C>T, c.2548+278C>T, c.2548+362A>C, c.282+79T>G **SLC35A3** c.469-119A>G, c.313+79A>G **MMAA** c.734-74G>A
HSD3B2 c.220G>A, c.308-177T>C, c.501G>A **LCA5** c.858+134G>T **CTNS** c.852+281T>C, c.852+259C>G
MCOLN1 c.1360-98A>G, c.1236+71G>A
USH2A c.4396+274C>A, c.4082-66A>C, c.4987+200C>T, c.12295-86G>C, c.9958+162T>C, c.2993+146A>G, c.12067-182C>G, c.1551-82T>C, c.8681+315A>G, c.848+103C>G, c.8223+203T>C, c.10586-196_10586-195dup, c.4628-136A>G, c.8559-65T>C, c.4628-261G>A, c.8681+120G>A, c.14582+196C>T, c.9372-95_9372-94dup, c.5298+82C>A, c.*18G>T, c.12067-117T>C, c.6486-185C>T, c.9371+205C>T, c.8224-218T>G, c.12294+134C>T, c.8846-35C>T
TSHR c.882-38G>A, c.393-9T>C, c.171-80T>A, c.468-69C>T **ASS1** c.495+84A>C, c.597+81A>G

CarrierSeq™ ECS

GALC c.1339-79A>G, c.621+94G>T, c.1671-162A>G, c.1835-204C>G, c.583-108G>A, c.1251+150C>T, c.1835-79A>G, c.1339-61C>T, c.1670+60C>T
SUCLA2 c.1107+97T>C, c.91-55G>A **ERCC3** c.823-108G>T, c.1828-38_1828-37del, c.1945+120A>G, c.471+52A>G
NPHS1 c.398-66T>C, c.1627+89A>G, c.397+61A>G, c.2816-16A>G **GLB1** c.1734+94C>T **NPHS2** c.535-97C>T **ERCC4** c.793-160C>T
MYO15A c.5532-47del, c.8602-76G>A, c.5407-63T>C, c.6764+93T>C, c.5212-65C>G, c.9708G>A **COL7A1** c.7759-98C>A
ERCC2 c.594+58C>T, c.594+90T>A, c.1832-70C>T, c.1426G>A, c.*96A>G, c.2191-81G>C, c.1831+61C>T
ERCC8 c.618-65G>A, c.618-91A>G, c.1041+98G>A **TRIM37** c.492+113A>G
ERCC5 c.264+121_264+122del, c.2678+91G>A, c.1954+108C>G **NAGS** c.916-57T>C **VPS45** c.261+481A>T, c.262-654G>A, c.622-16G>A
GLA c.639+68A>G

NA05117__CSeqVal_L1_T2.01_540_v2 (210 Genes 735 Variants)
SMARCAL1 c.2625+25C>A, c.2528+68T>C **MTRR** c.1557+95G>A **GLDC** c.1261+72G>A, c.1850+87T>A, c.2839-57A>G
MLC1 c.525+64G>A **AQP2** c.607-92A>G, c.526-54T>C
ABCA12 c.5940-156G>A, c.3295-142A>C, c.5940-168T>C, c.6118-78A>G, c.2472+137A>G, c.5129-68T>C, c.1657+72A>G, c.7680+78T>G, c.2684-113G>C, c.2684-138G>C, c.4383-70G>T, c.2472+90C>A
GLE1 c.322-35_322-29del **ZFYVE26** c.1640-177T>G, c.195-67T>G, c.1640-145C>T, c.4975-75C>T **AP1S1** c.430-186C>T
MMUT c.1083+57C>T, c.1808+66C>G, c.1677-53A>G **SLC12A6** c.1180+97C>A
EYS c.6078+68A>G, c.2846+53_2846+54insTAAT, c.2024-14delinsTT, c.1599+96A>C, c.6079-4_6079-3del
MCCC2 c.803+71C>T, c.1488+113G>A, c.1575-64A>G, g.71587309A>G, c.1488+103G>C **ARSA** c.624T>C
CPT1A c.693+35_693+37delinsAGCG **ALG6** c.494+74A>G **MCCC1** c.1978-57G>T, c.273+53A>C
HOGA1 c.212-21A>G, c.469-25C>T, c.604-85T>C
POR c.831-68C>G, c.1067-66T>C, c.1399-173G>A, c.366+89C>T, c.1399-34_1399-33delinsCT, c.1399-120G>A, c.238-95G>T, c.642-72G>A, c.1067-97C>T, c.831-55G>A, c.732-36C>T
BTD c.651C>T **TFR2** c.1995+92G>A, c.1996-111_1996-110insCA **BTK** c.1631+71C>T **HPD** c.831+53A>G
MMADHC c.372+54_372+55dup, c.-78G>C, c.696+83G>A **CFTR** c.*55_*85dup, c.224G>A, c.1210-13_1210-12del
CERKL c.1444-148G>C **GCDH** c.128-82T>G, c.-86A>G **SLC45A2** c.888+62_888+64del **RTEL1** c.-93C>T, c.369-104G>A
ABCB4 c.1732-39A>G
PCDH15 c.1910A>G, c.2092-168C>T, c.705+93C>T, c.1997+132T>G, c.3010-343_3010-342delinsCC, c.1918-165C>T, c.2092-148T>A, c.4202+125_4202+129delinsA, c.2091+229C>T, c.876+56T>G, c.594+232A>G, c.3984-170_3984-168del, c.1917+33_1917+34del, c.1997+169A>G, c.3717+194_3717+195del, c.986-208_986-205del, c.1997+244C>T
XPC c.901-70A>C, c.2605-51A>G **AAAS** c.1088-59A>G
PKHD1 c.667+57G>A, c.8107+81T>A, c.7733+63C>T, c.1234-174_1234-171dup, c.1234-174_1234-171del, c.7675G>C, c.7215+102T>A, c.5600+133G>C, c.7350+600G>A, c.8107+32G>A
GHRHR c.269-26G>T **RDH12** c.187+60G>A **HLCS** c.1796-66T>G **SURF1** c.752-65A>T
ABCA4 c.6729+61G>A, c.442+213T>C, c.5197-93C>T, c.5460+62G>A, c.442+80G>T, c.4352+54A>G **SLC6A8** c.395-96T>C, c.1141+87A>G
STAR c.65-59del **TH** c.1105-78A>G, c.91-54A>G **STRC** c.2480+75G>A, c.4779G>A, c.2784-62C>A, c.3498+234C>T
PAH c.969+221T>G, c.1065+155_1065+156delinsCG, c.60+134A>G, c.442-167A>G, c.706+302T>G, c.442-193A>G, c.1200-251C>T, c.912+229C>G, c.913-341A>G, c.843-268T>C, c.1200-186T>C, c.1066-236C>T, c.1066-193G>C
NDUFAF5 c.717+80A>G **PPT1** c.433+79A>G
ATM c.1066-294A>G, c.8787-55C>T, c.2467-123T>A, c.6006+191_6006+192del, c.7927+142G>A, c.8850+60A>G, c.7307+177T>G, c.2839-657G>A, c.4611+213A>G, c.496+221C>T, c.1899-242G>A, c.8671+104T>C, c.5006-170G>A, c.8786+90G>A, c.3993+197G>A, c.2250+221T>C, c.2839-90G>T, c.2377-56A>G
TECPR2 c.*60A>G **CC2D1A** c.*163G>C
PIGN c.674+163C>G, c.2619+86C>T, c.1860-36T>G, c.2370+186T>A, c.1574+56A>G, c.443-65C>T **HEXA** c.-226A>G
CHM c.116+80C>T, c.315-1543T>C, c.315-1455G>A **PYGM** c.528+74C>A, c.529-82G>A
IKBKAP c.1644-157_1644-156del, c.3856-82_3856-81delinsCT, c.1644-159_1644-156del **PEPD** c.259G>A
LYST c.7972+151A>G, c.10701+111dup **MED17** c.1584+113T>G, c.1329-71_1329-69delinsGAT
BBS9 c.702+121A>G, g.33635227-33635228, c.1538-91A>G, c.1330-62C>T **ACADM** c.118+133A>G, c.1044+99T>C, c.30+66C>T
LDLRAP1 c.712C>T, c.532+138_532+139del, c.617-102A>G **CTSD** c.827+111del
CTSC c.319-94dup, c.318+101A>T, c.318+53C>A, c.173-79A>T **BBS4** c.1248+68G>A, c.643-102T>C, c.332+150G>A, c.1036+114G>A
GP1BB c.*107C>T **ARG1** c.826+76dup **GAA** c.547-67C>G, c.2041-64G>A, c.956-84C>T, c.956-107G>A, c.1438-108G>A, c.1754+144C>T
ACAD9 c.1359-63T>C **F2** c.1726-59G>A **DDB2** c.456+65A>G **HADHB** c.1390-53T>G
HADHA c.68-82T>A, c.1393-62A>C, c.1221-195C>T
CYP21A2 c.357+39G>A, c.203-39_203-38delinsGG, c.203-44G>T, c.*52C>T, c.203-48A>G
IVD c.154-131_154-130del, c.153+56_153+80del, c.375+118A>G **AGPS** c.442-64C>T

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DPYD c.1740+140_1740+141insA, c.2908-58G>C, c.2908-69A>G **DLD** c.438+83G>A **CRB1** c.653-53T>G, c.3413+212T>C, c.1792+72A>G
FH c.1108+98C>A **GBA** c.762-180A>G, c.*102T>C, c.762-257C>T, c.*92G>A, c.1388+141A>G, c.1000-81A>C
COL11A2 c.607-61C>T, c.4135-119A>G, c.3108+52T>A, c.3702+151C>T, c.3757-82_3757-81inv, c.3217-83del **HSD17B3** c.278-67G>A
ABCB11 c.-27-50G>A, c.1638+80C>T, c.2343+127T>C
WRN c.3384-126T>C, c.2449-63A>G, c.3384-104T>A, c.210-52A>G, c.2968-65del, c.356-85C>T, c.1720+116C>A, c.2089-3168C>T, c.2631-67G>T, c.2089-3140T>A
CHRNG c.921-56C>G
DMD c.831+143_831+144insCA, c.30+125G>A, c.1483-72T>C, c.31+36949C>T, c.5448+169A>T, c.32-218C>T, c.2141+67G>A, c.3922-204C>G, c.5586+94_5586+95dup, c.2208-178G>A, c.6118-143C>A, c.7309+176T>C, c.7200+53C>G
AGA c.623-67_623-62dup **EVC2** c.3032+83A>G, c.1231-5T>C, c.3171delinsT, c.467-57T>C **GCH1** c.627-163G>A
GPR56 c.1299G>A, c.*74C>A, c.1167+77C>A **PET100** c.139-63_139-61del, c.114+75T>C, c.28-123A>G **AGL** c.665-73A>G
FAH c.707-107del, c.706+79A>G **LRPPRC** c.3451A>C **DCLRE1C** c.17+22_17+23delinsTA, c.1250T>G
MRE11 c.659+107A>G, c.846-60T>A, c.403-112T>C **MPL** c.1469-70T>C **SACS** c.6781C>A **SLC39A4** c.398T>C, c.1074+60G>A
LHCGR c.234-65A>T **HGD** c.342+70C>T **LIFR** c.1292-80T>A **RPGRIP1L** c.1104-82C>T **MAT1A** c.769-195T>A, c.951+98T>C
EDAR c.1025-101T>A, c.731-99C>T, c.655+30T>C, c.1024+44C>T **ALDH3A2** c.472-56G>A
PREPL c.1896+111T>C, c.1746+117C>T, c.1747-121T>G, c.616+108G>A, c.220-129A>G, c.752+228A>T, c.220-95C>T, c.616+80G>T, c.1156-160G>A, c.1896+168G>A, c.1746+136G>A, c.220-142C>A, c.969+259C>T, c.410-128_410-126del, c.752+82C>T
FAM161A c.1752-98del **COL4A4** c.694-72G>T, c.490-121T>G, c.1029+72G>A, c.2716+187C>T, c.4522+72G>A
DOK7 c.*105T>C, c.1109-54A>G, c.1262-116G>C **COL4A3** c.988-80T>C, c.324+73C>T **BLM** c.3559-95G>A, c.1883-129A>C
CYP19A1 c.146-148_146-144del, c.451+103_451+106dup, c.859-79A>G, c.146-59A>G, c.297-76A>G **ACAT1** c.940+84C>T
LOXHD1 c.1431+114T>G, c.416-107A>G, c.1654+69C>T, c.2048-102A>G **NLRP7** c.2726+98C>T, c.2388-67A>G, c.1725G>T
PSAP c.1431+78_1431+83del **NPHP1** c.1810+148G>A, c.1521-116C>T, c.1327-61C>T
CDH23 c.7722C>T, c.9319+72_9319+73insTC, c.5188-128T>A, c.3580-67G>A, c.9502C>T, c.5068-125G>T **SMN1** c.835-260C>T
PDHA1 c.172-84C>T **ATP8B1** c.1820-54T>A, c.2931+59T>A, c.3560_3562dup, c.555-167A>G
HPS1 c.507+61C>G, c.*154T>C, c.1398-130T>C
FANCA c.1470+305T>A, c.3626+216T>C, c.1901-62A>G, c.4010+92T>C, c.1084-181G>C, c.2779-54G>A, c.3514-67T>C, c.2602-156C>T, c.1626+163T>C, c.3935-102C>G, c.3627-203_3627-202delinsCT, c.1225+151T>C, c.1470+258T>C, c.2602-84G>A, c.2222+107T>C, c.1007-80C>T, c.3067-97T>C, c.1827-256A>G, c.1470+83G>A, c.1901-184A>G, c.1470+134_1470+145del, c.2151+159T>C, c.1901-205C>T, c.596+74G>A, c.2505-129G>C, c.2223-114C>T, c.3066+236C>G, c.1226-80T>C, c.596+143T>G, c.3240-146G>A, c.*245A>G, c.3067-114C>A, c.3514-184A>G, c.2505-236C>A, c.2222+100A>G, c.3067-57A>C, c.1471-119A>T, c.427-59A>G, c.2852+137T>C, c.1715+227G>A, c.1827-151A>C, c.3067-259G>T, c.2151+135A>G, c.3766-269C>T, c.3828+81G>T, c.1715+82T>C, c.*384A>T, c.3626+158G>A, c.-42-96_-42-84dup, c.3626+171A>G, c.2853-135A>G, c.1007-61del
HPS3 c.2107-57A>G, c.2107-52A>G, c.2888-42G>A, c.1163+62T>G, c.1692-192T>G
SLC4A11 c.778-31_778-29delinsCCAC, c.777+140C>A, c.1463+97T>G **ASNS** c.-23-44T>C, c.1477-32G>A, c.904-85A>G
FANCC c.997-216_997-215insATTATTT
NEB c.18997-173G>A, c.23649+282C>G, c.13993-32A>G, c.15451-32A>G, c.18997-193C>G, c.15555+325A>G, c.1675-67C>T, c.21418-296T>C, c.20049+337A>G, c.18366+78T>C, c.928-156T>C, c.14205+116C>G, c.19429-193T>C, c.21523-147A>G, c.1570-146A>T, c.10452+336G>A, c.2835+158A>G, c.718-250C>T, c.20368-57G>A, c.21840+82A>G, c.22590+237G>A, c.24393+60A>C, c.294+52T>G, c.19731+103G>T, c.2836-194G>A, c.24114+263_24114+266dup, c.19207-99dup, c.23241+303G>A, c.19836+213G>C, c.21522+78C>G, c.16909-168C>T, c.-30+205T>C, c.10452+71T>C, c.20466+148T>C, c.7536+188A>T, c.402+101A>G, c.18997-196A>G, c.21102+280C>G, c.15663+116C>G, c.24580-81A>G, c.17014-134T>C, c.927+335T>C, c.14097+325A>G, c.18471+201C>T, c.10452+202C>T, c.2835+215G>A
ACSF3 c.667-101T>C, c.667-77G>C, c.1239+57G>C, c.977+185T>C, c.823-7_823-6insCCGCCGCCGTGGGTCTCTGCCTGCTCATCTTCCTACCGAGTGCTTCCTTTCCT, c.978-83C>G, c.977+119A>G
FANCG c.84+77C>A **GH1** c.456+90T>A **SEPSECS** c.1026+89C>T **GRHPR** c.494-68A>G
CPS1 c.4101+62A>G, c.3337-79C>T, c.3481-8C>T
CYP11B2 c.955-77A>C, c.799+140C>T, c.799+127G>A, c.1122-60A>T, c.955-115_955-113delinsCG
CYP11B1 c.1122-197A>G, c.1122-126C>T, c.1120C>A, c.1122-60A>T, c.799+140C>T, c.799+119T>G, c.1122-80T>G, c.800-75T>G
ALPL c.862+58C>T **MAN2B1** c.1642-14C>T **DHCR7** c.831+69G>A **GALK1** c.611+56del, c.794-126T>C
ACADVL c.412-89T>C, c.412-92_412-76del **CIITA** c.3150-118A>G, c.2969+80C>A, c.359-67T>G **EDA** c.397-96293T>C
ITGB3 c.1914-139_1914-138insTG, c.2015-85T>C, c.1914-267G>T, c.2015-201A>G **TAT** c.408+58A>C, c.1042-72G>T
DYSF c.3348+63G>A, c.2055+105_2055+106del **ETFA** c.736-77_736-76insTAAGG, c.204+85dup, c.39+85C>G, c.39+80del
LAMC2 c.269-64C>T, c.196G>A, c.2457-115C>T, c.269-160C>T **NR2E3** c.119-28_119-13del
SGSH c.250-72G>A, g.80220458C>T, c.507-129G>A **SGCA** c.38-8C>T **OPA3** c.410A>T **AMH** c.864C>G
SLC37A4 g.119025405-119025406 **GUSB** c.724+25_724+26dup, c.724+98C>G, c.1477-68C>T, c.1391+504G>A **ATP7A** c.1543+86dup

CarrierSeq™ ECS

CEP290 c.6645+67G>A, c.853-127_853-125dup, c.442-56_442-54del **TSHB** c.163-112C>G **POLG** c.2734+39_2734+40insGTAG, c.-80C>T
DNAI2 c.1722+78G>A, c.865-66G>A **UGT1A1** c.-40_-39insTA, g.233758936A>C
VWF c.7549-59A>C, c.5053+130A>C, c.2282-122_2282-121inv, c.220+52T>C, c.5053+82C>T, c.5665-118G>A, c.1110-73T>A, c.5843-111A>G, c.2282-133T>C, c.5053+120G>C, c.1946-17_1946-15dup
ABCC8 c.4611+54G>C **ATRX** c.6110+22T>G **BCKDHB** c.952-151G>A
ABCC6 c.1867+60A>G, c.1431+73C>G, c.2995+142C>T, c.1177-94T>C, c.3633+55C>T, c.1868-57G>A, c.2787+62T>C, c.1177-89G>A
VPS13A c.144+236T>C, c.4956+124G>A, c.8472-12C>T, c.188-88_188-87insT, c.101-296C>T, c.3645C>A, c.3813-151A>T, c.5416-132A>G, c.2512+116A>G, c.283+269T>C, c.8035+371G>T, c.386-337C>T, c.7027-54A>G, c.990-203A>G, c.4412+215C>A, c.8908-149dup, c.8553+154A>G, c.556-94G>A, c.3118+66A>G, c.1161+134G>A, c.101-175_101-174del, c.9474+152C>T, c.2428-181A>G, c.9275+139G>C, c.*225T>C, c.4413-287C>T, c.101-62A>G
VPS13B c.2824+97G>C, c.3666+55T>C, c.4746-85C>T, c.5909-161G>A, c.2014-97C>G **POMGNT1** c.1212-81C>T, c.1212-66T>C
EVC c.385-84G>T, c.939+63C>A **HAX1** c.207A>T **NPC1** c.2605-70A>G **PCCA** c.637+102A>G **NDUFS6** c.187-53_187-50del
ACOX1 c.775-217C>T, c.1729-58A>C **PEX6** c.1688+88C>T, c.1368-177G>A, c.1689-60G>A **NDUFS4** c.351-101G>A
CNGB3 c.643+135A>T, c.339-139G>A, c.852+55C>T **AGXT** c.777-44A>G **ASPA** c.236+126T>C, c.236+153T>C
ATP6V1B1 c.274-72A>C, c.687+163G>A, c.1249-89C>T **CANT1** c.-342+53A>G
LAMA2 c.5727-24_5727-21delinsACTG, c.5071+3156A>G
DNAH5 c.4797-93C>A, c.3598+126A>G, c.11029-112C>T, c.1644+90C>A, c.4053+64G>A, c.4950+137C>T, c.4597-114_4597-113insCATATA, c.4355+60T>C, c.13491+66T>C, c.10281+118A>G, c.4054-59T>C, c.4796+57A>C
TYRP1 c.1409-67C>G **LAMA3** c.3089A>G **ETFDH** c.832-104A>C **USH1C** c.1260+83C>G, c.579+61G>A
SLC3A1 c.1137-201G>T, c.1011+203C>T, c.1137-317C>T, c.431-182G>A, c.765+155G>A, c.766-200G>A
SAMHD1 c.276-310G>T, c.276-105C>A, c.625+249G>T, c.1503+114_1503+115insAAGAAGTCATC **IL2RG** c.270-58A>G **CLN6** c.*131G>T
TTN c.87851T>C, c.16603A>T, c.10742-112A>T, c.13858+11101G>A, c.13859-6757G>A, c.39373G>A, c.7978+56G>A, c.32794G>T, c.9025+102C>A, c.8764+28_8764+29del, c.46886G>T, c.29781_29783dup, c.8764+13_8764+15del
CBS c.1105C>T **GALNT3** c.1626+131G>A
CTNS c.62-330A>G, c.970+70C>T, c.-19-211A>G, c.225+147G>C, c.141-103G>A, c.852+242_852+243delinsGG **MCOLN1** c.406-58G>A
USH2A c.11390-57C>T, c.1971+198A>G, c.6486-185C>T, c.1143+173C>G, c.11548+98G>A, c.485+83G>A, c.4082-66A>C, c.14583-359T>C, c.652-80T>C, c.848+103C>G, c.6163+155G>A, c.8559-65T>C, c.8681+315A>G
TSHR c.881+142T>C **ASS1** c.597+81A>G
GALC c.196-70G>A, c.753-59C>T, c.621+63T>A, c.1670+60C>T, c.622-121_622-118del, c.1671-162A>G, c.583-108G>T, c.1339-61C>T, c.752+56T>C, c.621+98T>C, c.752+120C>T, c.1835-79A>G, c.583-56G>A, c.582+99C>T, c.908+122G>A, c.1251+150C>T, c.1161+384C>T
PC c.1514-110G>A **SUCLA2** c.91-55G>A, c.1107+97T>C **ERCC3** c.1945+120A>G, c.823-108G>T, c.471+52A>G **ERCC4** c.793-160C>T
NPHS2 c.738+110T>A **MYO15A** c.5212-65C>G, c.5407-63T>C, c.6764+93T>C, c.8602-76G>A **COL7A1** c.5154+5T>C
ERCC8 c.1041+98G>A, c.1123-95A>G **NAGS** c.916-57T>C

Test Methods

CarrierSeq

Ion AmpliSeq targeted sequencing is used to analyze 14,044 amplicons covering the coding regions (CDS) of 420 genes including +/-25 bp flanking intron/exon boundaries, as well as selected intergenic, intronic and homologous regions. Note that the CDS regions were defined either by specific transcript or a combination of multiple transcripts. The targeted regions are sequenced with the aim to achieve a uniformity of ≥93%, aq20 mean read length of >155 basepairs, and coverage of >200X with the reads are aligned to human genome assembly GRCh38 (hg38). Targeted regions assess the potential of >36,000 putative carrier single nucleotide variants (SNVs) and insertion/deletions (indels) from the ClinVar archive of human variation and privately curated non-public variant sources. Variant calling is subject to quality control metrics including low read coverage. Variant calling of indels is limited in regions of homopolymer lengths of greater than eight nucleotides. Variant detection issues are possible in regions with low sequence complexity, large regional copy number changes, large indels, and regions with high homology to other genomic loci. Detection rates will be determined using analytical sensitivity, literature estimates for the disease allele contribution, and population frequency predictions. If variants have not been previously described in the literature, the detection rate might not be reported. Further, detection rates do not take into account the disease-specific rates of de novo mutation.

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Prediction Algorithms

SNV/indels

Variants with evidentiary support for inherited disorders using ClinVar and privately curated non-public variant sources will be reported. In addition, variants predicted to have a negative impact on gene function will be reported using modified variant classifications according to the American College of Medical Genetics and Genomics (ACMG) pathogenic criteria (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4544753/) evaluated as very strong (PVS1), strong (PS1), and benign criterion evaluated as stand-alone (BA1). When PVS1 criteria are met, the variant will be classified as “predicted to be pathogenic.” If PVS1 criteria are not met and PS1 classification is achieved, the variant will be classified as "predicted to be likely pathogenic". Using database population frequency estimates, when the criterion for BA1 is met and PVS1 and PS1 are not, the variant will be classified as "predicted to be benign". Finally, if all criteria are not achieved or found true for both PVS1\PS1 and BA1, the variant will be classified as a variant of unknown significance (VOUS).

Copy Number Variant (CNV) analysis

A read depth-based copy number analysis is used to analyze the amplicons targeting coding regions of the genes, as well as selected intergenic and intronic regions. CNV deletions will be classified "predicted to be likely pathogenic" and duplications are classified as VOUS. The precise breakpoints of large deletions in the target genes and intergenic regions cannot be determined, but are estimated from copy number analysis. Copy number calling requires three or more amplicons but algorithmic sensitivity to the single exon-level CNVs can be dependent on the coverage of the neighbouring region, amplicon proximity, and the size of the CNV event. Given the algorithmic requirements, a 1 kilobase CNV deletion in the focused CNV genes (30 targets) could potentially be detected in a single coding region segment with the exception of USH2A (CDS5); SLC3A1 (CDS9); PREPL (CDS2); NEB (CDS53, CDS74,82-85,91-93,98-101,160); VPS13A (CDS74); FANCC (CDS11); ATM (CDS11,42); PAH (CDS1,10); GALC (CDS1); HEXA (CDS1); CLN3 (CDS7); ITGB3 (CDS15); SAMHD1 (CDS1); DMD (CDS1, 8, 18, 26, 66, 83, 85); GLA (CDS4) Copy number event and variant analysis will be considered jointly for the genes GJB2 and GJB6, in the case of one parent with GJB2 variant and one parent with GJB6 deletion variant a risk state warning is issued. Genes that have closely related pseudogenes, highly related paralogues, or other homology-related issues may be addressed by different analysis methods (see special case gene analysis).

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Special case gene analysis

Algorithms use a combination of sequence read depth-based copy number analysis and SNV genotyping to determine the carrier status resulting from loss of function variants or deletion events or gene conversion events in certain genes that have high degrees of homology to other regions of the genome. Note that other variation or high copy numbers of pseudogenes or paralogues could interfere with this analysis.

SMN1

Targeted copy number and SNV genotyping analysis are used to determine the copy number of exon 7 of the SMN1 gene relative to highly homologous SMN2 gene. Additionally, some nondeletion variants in the SMN1 gene can be detected, however, de novo variants resulting in Spinal Muscular Atrophy (SMA) might not be detected by carrier screening. Of note, some individuals with two copies of SMN1 are silent carriers due to two SMN1 genes on one chromosome and an SMN1 deletion on the other chromosome (2+0 carrier status). The test genotypes g.27134T>G and c.*210_*211delTA SNVs, which increases the likelihood for silent 2+0 carriers in some ethnicities and as such positive samples are flagged for reproductive risk. Targeted genotyping of g.27134T>G SNV is only reported in individuals who have 2 copies or more of SMN1.

CYP21A2

A combination of sequence read depth-based copy number analysis and SNV genotyping are used to determine loss of function variants or gene conversion events for CYP21A2. The assay is able to detect the following variants: NM_000500.7:c.92C>T (p.Pro31Leu); NM_000500.7:c.293-13C>G; NM_000500.7:c.518T>A (p.Ile173Asn); NM_000500:c.597A>T (p.Leu199Phe); NM_000500.7:c.719T>A (p.Met240Lys); NM_000500.7:c.1360C>T (p.Pro454Ser). Targeted copy number testing of the CYP21A2 gene may not accurately determine non-classic 21-hydroxylase-deficient congenital adrenal hyperplasia (CAH) carrier status. Sensitivity to detect variants may be reduced if they result from complex gene conversion events. Additionally, variants within the context of di- or multi-nucleotide changes can lower the sensitivity of variant detection.

HBA1/2

The assay is able to detect CNV events in HBA1 and/or HBA2, resulting from -alpha20.5, --MED, --SEA, --FIL, -alpha3.7, -alpha4.2. Targeted copy number analysis for HBA1 and HBA2 attempts to name the CNV event, however, amplicon positions might not be able to distinguish between subtypes with copy number variants called as HBA1 or HBA2 deletions or several subtypes suggested. Detection of the breakpoints for overlapping CNV events may not be detected by this assay and sensitivity be limited to combinations of events with significantly differing boundaries. Read depth-based copy number analysis of HBA1/HBA2 may not be able to detect rare carrier states, in which complementary changes in this locus occur on the same chromosome with loss of copy number of an alpha-globin gene on the other chromosome.

GBA

A combination of sequence read depth-based copy number analysis and SNV genotyping are used to determine loss of function variants or gene conversion events for GBA. The assay is able to detect the following variants: NM_000157.3:c.680A>G (p.Asn227Ser); NM_000157.3:c.1448T>C (p.Leu483Pro); NM_001005741.2:c.1226A>G (p.Asn409Ser); NM_001005741.2:c.84dupG (p.Leu29Alafs*18); NM_001005741.2:c.115+1G>A (Splice donor); NM_001005741.2:c.1093G>A (p.Glu365Lys); NM_001005741.2:c.1361C>G (p.Pro454Arg). Sensitivity to detect these variants may be reduced if they result from complex gene conversion events. Additionally, variants within the context of di- or multi-nucleotide changes can lower the sensitivity to variant detection.

Reporting Variants

Variants are annotated using ClinVar and user-defined databases. Variants are classified according to the standards and guidelines for sequence variant interpretation established by the ACMG. Reported variant classifications are pathogenic and likely pathogenic. Reporting of VOUS is user-determined. Likely benign and benign variants are not reported. It is recommended to include user-defined variant reporting information in the lab comment section of the report. For further clarification, you should schedule genetic counselling.

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Limitations

CarrierSeq

Carrier Reporter and its results are For Research Use Only. Not for use in diagnostic procedures. The data presented here is a result of the curation of published data sources, but may not be exhaustive. A negative result, or no disease-causing variants detected, does not rule out the possibility of carrier status.

Appendices

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Best Regards

Lab User