ADVAT FOCUS – Carrier Screening

Patient name	:	**Mr. XXX**	**Mrs. YYY**
Gender/ Age	:	**Male/39 years**	**Female/37 years**
PIN	:	**XX**	**XX**
Sample no	:	**XX**	**XX**
Specimen	:	**XX**	**XX**
Sample collection date	:	**XX**	**XX**
Sample receipt date	:	**XX**	**XX**
Report date	:	**XX**	**XX**
Referring clinician	:	**XX**	
Hospital/Clinic	:	**XX**	

Clinical history

Mr. XXX and Mrs. YYY are second degree consanguineous couple with history of Recurrent Pregnancy Loss. Their first pregnancy (conceived throught ART) ended as a miscarriage and second pregnancy (Natural conception) was a biochemical pregnancy. Mr. XXXand Mrs. YYY have been evaluated for carrier status of pathogenic variations.

Risk Description

List of common uncertain significant carrier variant identified:

Disease	Mr. XXX	Mrs. YYY
	CARRIER	**CARRIER**
Hydatidiform mole, recurrent, 1 **(OMIM#231090)**	NM_001127255.1(*NLRP7*): c.1231G>A	NM_001127255.1 (*NLRP7*): c.1231G>A
Mode of inheritance: AR	p.Ala411Thr	p.Ala411Thr
	Heterozygous	Heterozygous
	Classification: **Uncertain Significance**	Classification: **Uncertain Significance**

*Genetic test results are reported based on the recommendation of American College of Medical Genetics [1].
No other variant that warrants to be reported for the given clinical indication was identified.

Interpretation

Interpretation for the common uncertain significant carrier variant identified in Mr. XXX and Mrs. YYY

***NLRP7*: c.1231G>A**

Variant summary: A heterozygous missense variation in exon 4 of the *NLRP7* gene (chr19:g.54939588C>T, NM_001127255.1, Depth: >100x) that results in the amino acid substitution of Threonine for Alanine at codon 411 (p.Ala411Thr) was detected.

Population frequency: This variant has minor allele frequency of 0.0026% in gnomAD database and has not been reported in 1000 genomes databases.

OMIM phenotype: Hydatidiform mole, recurrent, 1 (OMIM#231090) is caused by homozygous or compound heterozygous mutation in the *NLRP7* gene (OMIM*609661). This disease follows autosomal recessive pattern of inheritance [2].

Variant classification: Based on the evidence, this variant is classified as a variant of uncertain significance.

Recommendations

- The *NLRP7* gene has pseudogene in the human genome. Validation of the variant(s) by Sanger sequencing is strongly recommended to rule out false positives.
- Sequencing the variants in the parents and the other affected and unaffected members of the family is recommended to confirm the significance.
- Alternative test is strongly recommended to rule out the deletion/duplication.
- Genetic counseling is recommended.
- Validation of the variants by Sanger sequencing and MLPA is strongly recommended to rule out false positives.

Methodology

DNA extracted from the blood was used to perform ADVAT focus carrier screening test [3],[4],[5]. The targeted libraries were sequenced using targeted sequencing is used to analyze coding regions (CDS) of 420 genes. CDS regions were defined either by specific transcript or a combination of multiple transcripts. The targeted regions are to a targeted depth of 80 to 100X with the reads are aligned to human genome assembly GRCh38 (hg38). Detected variants were annotated and filtered using the ADVAT Focus software. 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. The variants were annotated using 1000 genomes(V2), gnomAD (v3.1.2,2.1.1), ClinVar, OMIM, dbSNP, NCBI RefSeq Genes. *In-silico* predictions of the variant was carried out using VS-SIFT, VS-PolyPhen2, PhyloP, GERP++, GeneSplicer, MaxEntScan, NNSplice, PWM Splice Predictor. Silent variations that do not result in any change in amino acid in the coding region are not reported.

Sequence data attributes

	Mr. XXX	Mrs. YYY
Total reads generated	11.74 Gb	10.62 Gb
Data ≥ Q30	99.66%	89.87%

Disclaimer

- Certain genes may not be covered completely, and few mutations could be missed. Variants not detected by this assay may impact the phenotype.
- Intronic variants, UTR, Promoter region variants and CNV are not assessed using this assay.
- The variations have not been validated by Sanger sequencing and MLPA.
- The above findings and result interpretation was done based on the clinical indication provided at the time of reporting.
- It is also possible that a pathogenic variant is present in a gene that was not selected for analysis and/or interpretation in cases where insufficient phenotypic information is available.
- Genes with paralog genes and genes with low complexity may have decreased sensitivity and specificity of variant detection and interpretation due to inability of the data and analysis tools to unambiguously determine the origin of the sequence data in such regions.
- The variants of uncertain significance and variations with high minor allele frequencies which are likely to be benign will be given upon request.

References

1. Richards, S, et al. Standards and Guidelines for the Interpretation of Sequence Variants: A Joint Consensus Recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genetics in medicine: official journal of the American College of Medical Genetics. 17.5 (2015): 405-424.
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3. Gao Z, et al. An estimate of the average number of recessive lethal mutations carried by humans. Genetics. 2015 Apr;199(4):1243-54. doi: 10.1534/genetics.114.173351. Epub 2015 Feb 18. PMID: 25697177; PMCID: PMC4391560.
4. Chong JX, et al. A population-based study of autosomal-recessive disease-causing mutations in a founder population. Am J Hum Genet. 2012 Oct 5;91(4):608-20. doi: 10.1016/j.ajhg.2012.08.007. Epub 2012 Sep 13. PMID: 22981120; PMCID: PMC3484657.

5. Gregg AR, et al. ACMG Professional Practice and Guidelines Committee. Screening for autosomal recessive and X-linked conditions during pregnancy and preconception: a practice resource of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2021 Oct;23(10):1793-1806. doi: 10.1038/s41436-021-01203-z. Epub 2021 Jul 20. Erratum in: Genet Med. 2021 Aug 27;: PMID: 34285390; PMCID: PMC8488021.

This report has been reviewed and approved by:

			
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APPENDIX: Current gene list used for carrier screening of pathogenic and likely pathogenic variants:

Disease Condition	Gene	Inhertiance \ Omim ID
Ataxia-Telangiectasia	*ATM*	AR \ 208900
Bardet-Biedl Syndrome 4	*BBS4*	AR \ 615982
Mental retardation, autosomal recessive 3	*CC2D1A*	AR \ 608443
Cystic Fibrosis	*CFTR*	AR \ 219700
Ceroid Lipofuscinosis, Neuronal, 3	*CLN3*	AR \ 204200
Cystinosis	*CTNS*	AR \ 219800, 219900, 219750
Duchenne/Becker Muscular Dystrophy	*DMD*	XLR \ 310200
Fanconi Anemia, Group A	*FANCA*	AR \ 227650
Fanconi Anemia, Group C	*FANCC*	AR \ 227645
Glycogen Storage Disease, Type II (Pompe Disease)	*GAA*	AR \ 232300
Krabbe Disease	*GALC*	AR \ 245200
Galactosemia	*GALT*	AR \ 230400
Isolated growth hormone deficiency, Type IA/II	*GH1*	AR \ 262400
Non-Syndromic Hearing Loss (a.k.a. Connexin 26)	*GJB2*	AR \ 220290
Non-Syndromic Hearing Loss (a.k.a. Connexin 30)	*GJB6*	AR \ 220290 ,612645
Fabry Disease	*GLA*	XL \ 301500
Beta-Hemoglobinopathies	*HBB*	\ 613985
Tay-Sachs Disease	*HEXA*	AR \ 272800
Glanzmann thrombasthenia	*ITGB3*	AR \ 619267
Mucolipidosis, Type IV	*MCOLN1*	AR \ 252650
Nemaline Myopathy, NEB-Related	*NEB*	AR \ 256030
Phenylketonuria	*PAH*	AR \ 261600
Usher Syndrome, Type 1F	*PCDH15*	AR \ 602083
Myasthenic syndrome, congenital, 22	*PREPL*	AR \ 616224
Aicardi-Goutières Syndrome	*SAMHD1*	AR \ 612952
Cystinuria, Type A	*SLC3A1*	AR,AD \ 220100
Deafness, autosomal recessive 16	*STRC*	AR \ 603720
Usher Syndrome, Type 2A	*USH2A*	AR \ 276901
Choreo-acanthocytosis	*VPS13A*	AR \ 200150
Congenital Adrenal Hyperplasia, 21-hydroxylase-deficient	*CYP21A2*	AR \ 201910
Alpha-Thalassemia	*HBA1*	\ 604131
Alpha-Thalassemia	*HBA2*	\ 604131
Spinal Muscular Atrophy	*SMN1*	AR \ 253300 , 253550 ,253400, 271150
Achalasia-Addisonianism-Alacrima Syndrome	*AAAS*	AR \ 231550
Harlequin ichthyosis	*ABCA12*	AR \ 242500
Stargardt Disease, Type 1	*ABCA4*	AR \ 248200
Progressive Familial Intrahepatic Cholestasis, Type 2	*ABCB11*	AR \ 601847
Progressive Familial Intrahepatic Cholestasis, Type 3	*ABCB4*	AR \ 602347

Pseudoxanthoma elasticum	*ABCC6*	AR \ 264800
Familial Hyperinsulinism, ABCC8-Related	*ABCC8*	AD, AR \ 256450
Adrenoleukodystrophy, X-Linked	*ABCD1*	XLR \ 300100
Mitochondrial Complex I Deficiency, ACAD9-Related	*ACAD9*	AR \ 611126
Medium Chain Acyl-CoA Dehydrogenase Deficiency	*ACADM*	AR \ 201450
Short Chain Acyl-CoA Dehydrogenase Deficiency	*ACADS*	AR \ 201470
Short/branched chain acyl-CoA dehydrogenase	*ACADSB*	AR \ 610006
Very Long-Chain Acyl-CoA Dehydrogenase Deficiency	*ACADVL*	AR \ 201475
Beta-Ketothiolase Deficiency	*ACAT1*	AR \ 203750
Acyl-CoA Oxidase I Deficiency	*ACOX1*	AR \ 264470
Combined Malonic and Methylmalonic Aciduria	*ACSF3*	AR \ 614265
Severe Combined Immunodeficiency, ADA-Related	*ADA*	AR,So \ 102700
Ehlers-Danlos Syndrome, Type VIIC	*ADAMTS2*	AR \ 225410
Bilateral Frontoparietal Polymicrogyria	*ADGRG1*	AR \ 606854
Aspartylglucosaminuria	*AGA*	AR \ 208400
Glycogen Storage Disease, Type III (Cori/Forbes)	*AGL*	AR \ 232400
Rhizomelic Chondrodysplasia Punctata, Type 3	*AGPS*	AR \ 600121
Hyperoxaluria, Primary, Type 1	*AGXT*	AR \ 259900
Autoimmune polyendocrinopathy syndrome, type I	*AIRE*	AD, AR \ 240300
Sjogren-Larsson Syndrome	*ALDH3A2*	AR \ 270200
Pyridoxine-dependent epilepsy	*ALDH7A1*	AR \ 266100
Hereditary Fructose Intolerance	*ALDOB*	AR \ 229600
Congenital Disorder of Glycosylation, Type 1C	*ALG6*	AR \ 603147
Alstrom Syndrome	*ALMS1*	AR \ 203800
Hypophosphatasia, ALPL-Related	*ALPL*	AD, AR \ 146300 ,241510 , 241500, 146300
Persistent Müllerian duct syndrome type 1	*AMH*	AR \ 261550
Persistent Müllerian duct syndrome type 2	*AMHR2*	AR \ 261550
Glycine Encephalopathy, AMT-Related	*AMT*	\ 620398
Mental retardation, enteropathy, deafness, peripheral neuropathy, ichthyosis, and keratoderma (MEDNIK)	*AP1S1*	AR \ 609313
Familial Nephrogenic Diabetes Insipidus, AQP2-Related	*AQP2*	AD, AR \ 125800
Androgen insensitivity syndrome, X-Linked	*AR*	XLR \ 300068
Argininemia	*ARG1*	AR \ 207800
Metachromatic Leukodystrophy, ARSA-Related	*ARSA*	AR \ 250100
Mucopolysaccharidosis, Type VI (Maroteaux-Lamy)	*ARSB*	AR \ 253200
Argininosuccinate Lyase Deficiency	*ASL*	AR \ 207900
Asparagine Synthetase Deficiency	*ASNS*	AR \ 615574
Canavan Disease	*ASPA*	AR \ 271900
Citrullinemia, Type 1	*ASS1*	AR \ 215700
Renal Tubular Acidosis and Deafness, ATP6V1B1-Related	*ATP6V1B1*	AR \ 267300
Menkes Syndrome, X-Linked	*ATP7A*	AR \ 309400
Wilson Disease	*ATP7B*	AR \ 277900

Progressive Familial Intrahepatic Cholestasis, Type 1	*ATP8B1*	AR \ 211600
Alpha-Thalassemia Intellectual Disability Syndrome, X-Linked	*ATRX*	XLD \ 301040
Bardet-Biedl Syndrome 1	*BBS1*	AR, DR \ 209900
Bardet-Biedl Syndrome 10	*BBS10*	AR \ 615987
Bardet-Biedl Syndrome 12	*BBS12*	AR \ 615989
Bardet-Biedl Syndrome 2	*BBS2*	AR \ 615981
Bardet-Biedl Syndrome 9	*BBS9*	AR \ 615986
Pseudocholinesterase Deficiency	*BCHE*	AR \ 617936
Maple Syrup Urine Disease, Type 1A	*BCKDHA*	AR \ 248600
Maple Syrup Urine Disease, Type 1B	*BCKDHB*	AR \ 620698
GRACILE Syndrome	*BCS1L*	AR \ 603358
Bloom Syndrome	*BLM*	AR \ 210900
Fanconi anemia, Group J	*BRIP1*	\ 609054
Bartter syndrome, Type 4a	*BSND*	AR \ 602522
Biotinidase Deficiency	*BTD*	AR \ 253260
Isolated growth hormone deficiency, Type III, X-linked	*BTK*	XLR \ 307200
Desbuquois dysplasia 1	*CANT1*	AR \ 251450
Limb-Girdle Muscular Dystrophy, Type 2A	*CAPN3*	AR \ 253600
Catecholaminergic polymorphic ventricular tachycardia	*CASQ2*	AR \ 611938
Homocystinuria, CBS-Related	*CBS*	AR \ 236200
Usher Syndrome, Type 1D	*CDH23*	AR, DR \ 601067
Leber Congenital Amaurosis, Type CEP290	*CEP290*	\ 611755
Retinitis Pigmentosa 26	*CERKL*	AR \ 608380
Choroideremia, X-Linked	*CHM*	XL \ 303100
Congenital Myasthenic Syndrome, CHRNE-Related	*CHRNE*	AD, AR \ 605809, 616324, 608931
Escobar Syndrome	*CHRNG*	AR \ 265000
Bare Lymphocyte Syndrome, CIITA-Related	*CIITA*	AR \ 209920
Ceroid Lipofuscinosis, Neuronal, 5	*CLN5*	AR \ 256731
Ceroid Lipofuscinosis, Neuronal, 6	*CLN6*	AR \ 601780, 204300
Ceroid Lipofuscinosis, Neuronal, 8 (a.ka. Northern Epilepsy)	*CLN8*	AR \ 610003
Usher Syndrome, Type 3	*CLRN1*	AR \ 276902
Achromatopsia, CNGA3-Related	*CNGA3*	AR \ 216900
Achromatopsia, CNGB3-Related	*CNGB3*	AR \ 262300
Fibrochondrogenesis type 2	*COL11A2*	AD, AR \ 614524
Alport Syndrome, COL4A3-Related	*COL4A3*	AR \ 620536
Alport Syndrome, COL4A4-Related	*COL4A4*	AR \ 203780
Alport Syndrome, X-Linked	*COL4A5*	XLD \ 301050
Dystrophic Epidermolysis Bullosa, COL7A1-Related	*COL7A1*	AR \ 226600
Carbamoyl Phosphate Synthetase I Deficiency	*CPS1*	AR \ 237300
Carnitine Palmitoyltransferase IA Deficiency	*CPT1A*	AR \ 255120
Carnitine Palmitoyltransferase II Deficiency	*CPT2*	AD, AR \ 600649, 600649, 255110

Leber congenital amaurosis 8	*CRB1*	AR \ 613835
Papillon-Lefevre Syndrome	*CTSC*	AR \ 245000
Ceroid Lipofuscinosis, Neuronal, 10 (CLN10 Disease)	*CTSD*	AR \ 610127
Pycnodysostosis	*CTSK*	AR \ 265800
Chronic Granulomatous Disease, CYBA-Related	*CYBA*	AR \ 233690
Chronic Granulomatous Disease, X-Linked	*CYBB*	XLR \ 306400
Congenital Adrenal Hyperplasia, 11-beta-hydroxylase-deficient	*CYP11B1*	AR \ 202010
Corticosterone Methyloxidase Deficiency	*CYP11B2*	AR \ 203400, 610600
Congenital Adrenal Hyperplasia, 17-Alpha-Hydroxylase Deficiency	*CYP17A1*	AR \ 202110
Aromatase Deficiency	*CYP19A1*	\ 613546
Primary Congenital Glaucoma	*CYP1B1*	AR \ 231300
Cerebrotendinous Xanthomatosis	*CYP27A1*	AR \ 213700
Vitamin D-dependent rickets type 1A	*CYP27B1*	AR \ 264700
Maple Syrup Urine Disease, Type 2	*DBT*	AR \ 620699
Severe Combined Immunodeficiency, Type Athabaskan	*DCLRE1C*	AR \ 602450
Xeroderma Pigmentosum Group E	*DDB2*	AR \ 278740
Smith-Lemli-Opitz Syndrome	*DHCR7*	AR \ 270400
Retinitis Pigmentosa 59	*DHDDS*	AR \ 613861
Dyskeratosis congenita, X-Linked	*DKC1*	AR \ 305000
Dihydrolipoamide Dehydrogenase Deficiency	*DLD*	AR \ 246900
Ciliary Dyskinesia, Primary 3	*DNAH5*	AR \ 608644
Ciliary Dyskinesia, Primary 1	*DNAI1*	AR \ 244400
Ciliary Dyskinesia, Primary 9	*DNAI2*	AR \ 612444
Ciliary Dyskinesia, Primary, 16	*DNAL1*	AR \ 614017
Congenital Myasthenic Syndrome, DOK7-Related	*DOK7*	AR \ 254300
Dihydropyrimidine Dehydrogenase Deficiency	*DPYD*	AR \ 274270
Limb-Girdle Muscular Dystrophy, Type 2B	*DYSF*	AR \ 253601
Hypohidrotic Ectodermal Dysplasia, X-Linked	*EDA*	AR \ 305100
Hypohidrotic Ectodermal Dysplasia	*EDAR*	AR \ 224900
Wolcott-Rallison Syndrome	*EIF2AK3*	AR \ 226980
Leukoencephalopathy with Vanishing White Matter	*EIF2B5*	AR \ 620315
Dysautonomia, familial (IKBKAP or ELP1)	*IKBKAP*	AR \ 223900
Emery-Dreifuss Muscular Dystrophy 1, X-Linked	*EMD*	XLR \ 310300
Xeroderma Pigmentosum Group D	*ERCC2*	AR \ 278730
Xeroderma Pigmentosum Group B	*ERCC3*	AR \ 610651
Xeroderma Pigmentosum Group F	*ERCC4*	AR \ 278760
Xeroderma pigmentosum Group G	*ERCC5*	AR \ 278780
Cockayne syndrome, type B	*ERCC6*	AR \ 133540
Cockayne syndrome, type A	*ERCC8*	AR \ 216400
Roberts Syndrome	*ESCO2*	AR \ 268300
Glutaric Acidemia, Type 2A	*ETFA*	AR \ 231680

Glutaric Acidemia, Type 2B	*ETFB*	AR \ 231680
Glutaric Acidemia, Type 2C	*ETFDH*	AR \ 231680
Ethylmalonic Encephalopathy	*ETHE1*	AR \ 602473
Ellis-van Creveld Syndrome, EVC-Related	*EVC*	AR \ 225500
Ellis-van Creveld Syndrome, EVC2-related	*EVC2*	AR \ 225500
Pontocerebellar Hypoplasia, Type 1B	*EXOSC3*	AR \ 614678
Retinitis Pigmentosa 25	*EYS*	AR \ 602772
Factor XI deficiency	*F11*	AR \ 612416
Prothrombin deficiency	*F2*	AR \ 613679
Hemophilia A	*F8*	XLR \ 306700
Hemophilia B	*F9*	XLR \ 306900
Tyrosinemia, Type I	*FAH*	AR \ 276700
Retinitis Pigmentosa 28	*FAM161A*	AR \ 606068
Fanconi Anemia, Group G	*FANCG*	AR \ 614082
Fumarase Deficiency	*FH*	AR \ 606812
Limb-Girdle Muscular Dystrophy, Type 2I	*FKRP*	AR \ 607155
Walker-Warburg Syndrome, FKTN-Related	*FKTN*	AR \ 253800
Glycogen Storage Disease, Type IA	*G6PC*	AR \ 232200
Glucose-6-Phosphate Dehydrogenase Deficiency*	*G6PD*	AR \ 300908
Galactose epimerase deficiency	*GALE*	AR \ 230350
Galactokinase Deficiency (Galactosemia, Type II)	*GALK1*	AR \ 230200
Mucopolysaccharidosis, Type IVA	*GALNS*	AR \ 253000
Hyperphosphatemic familial tumoral calcinosis	*GALNT3*	AR \ 211900
Guanidinoacetate Methyltransferase Deficiency	*GAMT*	AR \ 612736
Gaucher Disease	*GBA*	AR \ 230800, 230900 , 231000, 231005
Glycogen Storage Disease, Type IV	*GBE1*	AR \ 232500
Glutaric Acidemia, Type 1	*GCDH*	AR \ 231670
Dopa-responsive dystonia	*GCH1*	AD,AR \ 128230
Grebe syndrome	*GDF5*	AR \ 200700
Combined Oxidative Phosphorylation Deficiency 1	*GFM1*	AR \ 609060
Isolated growth hormone deficiency, Type IB	*GHRHR*	AR \ 618157
Charcot-Marie-Tooth Disease with Deafness, X-Linked	*GJB1*	XLD \ 302800
Erythrokeratodermia variabilis et progressiva	*GJB3*	AD,AR \ 133200
Mucopolysaccharidosis, Type IVB / GM1 Gangliosidosis	*GLB1*	AR \ 253010
Glycine Encephalopathy, GLDC-Related	*GLDC*	AR \ 605899
Lethal Congenital Contracture Syndrome 1	*GLE1*	AR \ 253310
Inclusion Body Myopathy 2	*GNE*	AR \ 620757
Mucolipidosis II/IIIA	*GNPTAB*	AR \ 252500, 252600
Mucolipidosis III gamma	*GNPTG*	AR \ 252605
Mucopolysaccharidosis, Type IIID (Sanfilippo D)	*GNS*	AR \ 252940
Geroderma osteodysplastica	*GORAB*	AR \ 231070

Bernard-Soulier Syndrome, Type A2	*GP1BA*	AD \ 153670
Bernard-Soulier Syndrome, Type B	*GP1BB*	AR \ 231200
Bernard-Soulier Syndrome, Type C	*GP9*	AR \ 231200
Primary Hyperoxaluria, Type 2	*GRHPR*	AR \ 260000
Leber congenital amaurosis 1	*GUCY2D*	AR \ 204000
Mucopolysaccharidosis, Type VII	*GUSB*	AR \ 253220
Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	*HADHA*	AR \ 609016
Trifunctional protein deficiency	*HADHB*	AR \ 620300
Congenital Neutropenia, HAX1-Related	*HAX1*	AR \ 610738
Sandhoff Disease	*HEXB*	AR \ 268800
Hemochromatosis, Type 1	*HFE*	AR \ 235200
Hemochromatosis, Type 2A	*HFE2*	AR \ 602390
Alkaptonuria	*HGD*	AR \ 203500
Mucopolysaccharidosis, Type IIIC (Sanfilippo C)	*HGSNAT*	AR \ 252930
Holocarboxylase Synthetase Deficiency	*HLCS*	AR \ 253270
3-Hydroxy-3-Methylglutaryl-Coenzyme A Lyase Deficiency	*HMGCL*	AR \ 246450
Heme Oxygenase-1 Deficiency	*HMOX1*	AR \ 614034
Primary Hyperoxaluria, Type 3	*HOGA1*	AR \ 613616
Tyrosinemia, Type III	*HPD*	AR \ 276710
Hermansky-Pudlak Syndrome 1	*HPS1*	AR \ 203300
Hermansky-Pudlak Syndrome 3	*HPS3*	AR \ 614072
Hermansky-Pudlak syndrome 4	*HPS4*	AR \ 614073
17-beta hydroxysteroid dehydrogenase 3 deficiency	*HSD17B3*	AR \ 264300
D-Bifunctional Protein Deficiency	*HSD17B4*	AR \ 261515
3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	*HSD3B2*	AR \ 201810
Hydrolethalus Syndrome	*HYLS1*	AR \ 236680
Mucopolysaccharidosis, Type II (Hunter Syndrome)	*IDS*	XLR \ 309900
Mucopolysaccharidosis, Type I (Hurler Syndrome)	*IDUA*	AR \ 607014
Severe Combined Immunodeficiency, X-Linked	*IL2RG*	XLR \ 300400
Isovaleric Acidemia	*IVD*	AR \ 243500
Congenital Hyperinsulinism, KCNJ11-Related	*KCNJ11*	AD,AR \ 601820
LAMA2-related Muscular Dystrophy	*LAMA2*	AR \ 607855, 618138
Herlitz Junctional Epidermolysis Bullosa, LAMA3-Related	*LAMA3*	AR \ 619783, 619784, 245660
Herlitz Junctional Epidermolysis Bullosa, LAMB3-Related	*LAMB3*	AR \ 104530, 226650, 226700
Herlitz Junctional Epidermolysis Bullosa, LAMC2-Related	*LAMC2*	AR \ 619785 , 619786
Leber Congenital Amaurosis, Type LCA5	*LCA5*	AR \ 604537
Familial Hypercholesterolemia, LDLR-Related	*LDLR*	AD,AR \ 143890
Familial Hypercholesterolemia, LDLRAP1-Related	*LDLRAP1*	AR \ 603813
Leydig cell hypoplasia	*LHCGR*	AR \ 176410, 238320, 238320, 238320
Stuve-Wiedemann Syndrome	*LIFR*	AR \ 601559
Lysosomal Acid Lipase Deficiency	*LIPA*	AR \ 278000, 620151

Woolly Hair/Hypotrichosis Syndrome	*LIPH*	AR \ 604379
Deafness, Autosomal Recessive 77	*LOXHD1*	AR \ 613079
Lipoprotein Lipase Deficiency	*LPL*	AR \ 238600
Leigh Syndrome, French-Canadian Type	*LRPPRC*	AR \ 220111
Chediak-Higashi syndrome	*LYST*	AR \ 214500
Alpha-Mannosidosis	*MAN2B1*	AR \ 248500
Hypermethioninemia	*MAT1A*	AR \ 250850
3-Methylcrotonyl-CoA Carboxylase 1 Deficiency	*MCCC1*	AR \ 210200
3-Methylcrotonyl-CoA Carboxylase 2 Deficiency	*MCCC2*	AR \ 210210
RETT Syndrome	*MECP2*	XLD \ 312750
Microcephaly, postnatal progressive, with seizures and brain atrophy	*MED17*	AR \ 613668
Familial Mediterranean Fever	*MEFV*	AR \ 249100
Spondylothoracic Dysostosis, MESP2-Related	*MESP2*	AR \ 608681
Ceroid Lipofuscinosis, Neuronal, 7	*MFSD8*	AR \ 610951
Bardet-Biedl Syndrome 6	*MKKS*	AR \ 605231
Meckel-Gruber Syndrome, Type 1	*MKS1*	AR \ 249000
Megalencephalic Leukoencephalopathy with Subcortical Cysts	*MLC1*	AR \ 604004
Malonyl-CoA decarboxylase deficiency	*MLYCD*	AR \ 248360
Methylmalonic Aciduria, MMAA-Related	*MMAA*	AR \ 251100
Methylmalonic Aciduria, MMAB-Related	*MMAB*	AR \ 251110
Methylmalonic Aciduria and Homocystinuria, Type cblC	*MMACHC*	AR \ 277400
Methylmalonic Aciduria and Homocystinuria, Type cblD	*MMADHC*	AR \ 277410
Molybdenum cofactor deficiency	*MOCS1*	AR \ 252150
Congenital Disorder of Glycosylation, Type 1B	*MPI*	AR \ 602579
Congenital Amegakaryocytic Thrombocytopenia	*MPL*	AR \ 604498
Hepatocerebral Mitochondrial DNA Depletion Syndrome, MPV17-Related	*MPV17*	AR \ 256810
Ataxia-telangiectasia-like disorder 1	*MRE11*	AR \ 604391
Homocystinuria due to Deficiency of MTHFR	*MTHFR*	AR \ 236250
Myotubular Myopathy, X-Linked	*MTM1*	XLR \ 310400
Homocystinuria, Type cblE	*MTRR*	AR \ 236270
Abetalipoproteinemia	*MTTP*	AR \ 200100
Methylmalonic Aciduria, Type mut(0)	*MUT*	AR \ 251000
Deafness, autosomal recessive, 3	*MYO15A*	AR \ 600316
Usher Syndrome, Type 1B	*MYO7A*	AR \ 276900
Mucopolysaccharidosis, Type IIIB (Sanfilippo B)	*NAGLU*	AR \ 252920
N-acetylglutamate Synthase Deficiency	*NAGS*	AR \ 237310
Nijmegen Breakage Syndrome	*NBN*	AR \ 251260
Charcot-Marie-Tooth Disease type 4D	*NDRG1*	AR \ 601455
Mitochondrial Complex I Deficiency, NDUFAF5-Related	*NDUFAF5*	AR \ 618238
Mitochondrial complex I deficiency	*NDUFS4*	AR \ 252010
Mitochondrial Complex I Deficiency, NDUFS6-Related	*NDUFS6*	AR \ 618232

Sialidosis	*NEU1*	AR \ 256550
Hydatidiform Mole, Recurrent	*NLRP7*	AR \ 231090
Niemann-Pick Disease, Type C1/D	*NPC1*	AR \ 257220
Niemann-Pick Disease, Type C2	*NPC2*	AR \ 607625
Juvenile Nephronophthisis	*NPHP1*	AR \ 256100
Congenital Finnish Nephrosis	*NPHS1*	AR \ 256300
Steroid-Resistant Nephrotic Syndrome	*NPHS2*	AR \ 600995
Congenital Adrenal Hypoplasia, X-linked	*NR0B1*	XLR \ 300200
Enhanced S-Cone Syndrome	*NR2E3*	AR \ 268100
Congenital Insensitivity to Pain with Anhidrosis (CIPA)	*NTRK1*	AR \ 256800
Ornithine Aminotransferase Deficiency	*OAT*	AR \ 258870
Lowe syndrome, X-Linked	*OCRL*	XLR \ 309000
Costeff Syndrome (3-Methylglutaconic Aciduria, Type 3)	*OPA3*	AR \ 258501
Ornithine Transcarbamylase Deficiency	*OTC*	XL \ 311250
Pantothenate Kinase-Associated Neurodegeneration	*PANK2*	AR \ 234200
Pyruvate Carboxylase Deficiency	*PC*	AR \ 266150
Propionic Acidemia, PCCA-Related	*PCCA*	AR \ 606054
Propionic Acidemia, PCCB-Related	*PCCB*	AR \ 606054
Pyruvate Dehydrogenase Deficiency, X-Linked	*PDHA1*	XLD \ 312170
Pyruvate Dehydrogenase Deficiency, PDHB-Related	*PDHB*	AR \ 614111
Prolidase deficiency	*PEPD*	AR \ 170100
Cytochrome-c oxidase deficiency	*PET100*	AR \ 619055
Peroxisome Biogenesis Disorder 1A (Zellweger)	*PEX1*	AR \ 214100
Peroxisome Biogenesis Disorder 6A (Zellweger)	*PEX10*	AR \ 614870
Peroxisome Biogenesis Disorder 3A (Zellweger)	*PEX12*	AR \ 614859
Peroxisome Biogenesis Disorder 5A (Zellweger)	*PEX2*	AR \ 614866
Peroxisome Biogenesis Disorder 4A (Zellweger)	*PEX6*	AR \ 614862
Rhizomelic Chondrodysplasia Punctata, Type 1	*PEX7*	AR \ 215100
Glycogen Storage Disease, Type VII	*PFKM*	AR \ 232800
Phosphoglycerate Dehydrogenase Deficiency	*PHGDH*	AR \ 601815
Multiple congenital anomalies-hypotonia-seizures syndrome 1	*PIGN*	AR \ 614080
Polycystic Kidney Disease, Autosomal Recessive	*PKHD1*	AR \ 263200
Infantile neuroaxonal dystrophy 1	*PLA2G6*	AR \ 256600
Congenital Disorder of Glycosylation, Type 1A, PMM2-Related	*PMM2*	AR \ 212065
Pyridoxal 5'-phosphate-dependent epilepsy	*PNPO*	AR \ 610090
POLG-Related Disorders	*POLG*	AR \ 203700, 613662, 607459, 258450
Xeroderma pigmentosum Variant	*POLH*	AR \ 278750
Muscle-Eye-Brain Disease, POMGNT1-Related	*POMGNT1*	AR \ 253280
Cytochrome P450 oxidoreductase deficiency	*POR*	AR \ 613571
Ceroid Lipofuscinosis, Neuronal, 1	*PPT1*	AR \ 256730
Combined Pituitary Hormone Deficiency 2	*PROP1*	AR \ 262600

Arts syndrome, X-Linked	*PRPS1*	AR \ 301835
Metachromatic Leukodystrophy, PSAP-Related	*PSAP*	AR \ 249900
6-Pyruvoyl-Tetrahydropterin Synthase (PTPS) Deficiency	*PTS*	AR \ 261640
Mitochondrial Myopathy and Sideroblastic Anemia (MLASA1)	*PUS1*	AR \ 600462
Glycogen Storage Disease, Type V (McArdle Disease)	*PYGM*	AR \ 232600
Carpenter Syndrome	*RAB23*	AR \ 201000
Omenn Syndrome, RAG1-Related	*RAG1*	AR \ 603554
Omenn Syndrome, RAG2-Related	*RAG2*	AR \ 603554
Congenital Myasthenic Syndrome, RAPSN-Related	*RAPSN*	AR \ 616326
Pontocerebellar Hypoplasia, Type 1 and 6, RARS2-Related	*RARS2*	AR \ 611523
Leber Congenital Amaurosis, Type RDH12	*RDH12*	AD,AR \ 612712
Retinal Dystrophies, RLBP1-Associated	*RLBP1*	AD,AR \ 607475, 136880, 607476, 136880
Cartilage-Hair Hypoplasia	*RMRP*	AR \ 250250
Aicardi-Goutieres syndrome, RNASEH2C-related	*RNASEH2C*	AR \ 610329
Leber Congenital Amaurosis 2	*RPE65*	AR \ 204100
Juvenile Retinoschisis, X-Linked	*RS1*	XLR \ 312700
Dyskeratosis Congenita, RTEL1-Related	*RTEL1*	AD,AR \ 615190
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	*SACS*	AR \ 270550
MIRAGE syndrome	*SAMD9*	AD \ 617053
Shwachman-Diamond syndrome	*SBDS*	AR \ 260400
Pontocerebellar Hypoplasia, Type 2D	*SEPSECS*	AR \ 613811
Alpha-1-Antitrypsin Deficiency	*SERPINA1*	AR \ 613490
Limb-Girdle Muscular Dystrophy, Type 2D	*SGCA*	AR \ 608099
Limb-Girdle Muscular Dystrophy, Type 2E	*SGCB*	AR \ 604286
Limb-Girdle Muscular Dystrophy, Type 2F	*SGCD*	AR \ 601287
Limb-Girdle Muscular Dystrophy, Type 2C	*SGCG*	AR \ 253700
Mucopolysaccharidosis, Type IIIA (Sanfilippo A)	*SGSH*	AR \ 252900
Gitelman Syndrome	*SLC12A3*	AR \ 263800
Agenesis of the Corpus Callosum with Peripheral Neuropathy (Andermann Syndrome)	*SLC12A6*	AR \ 218000
Salla Disease	*SLC17A5*	AR \ 604369
Megaloblastic Anemia Syndrome	*SLC19A2*	AR \ 249270
Carnitine Deficiency	*SLC22A5*	AR \ 212140
Citrullinemia, Type II	*SLC25A13*	AR \ 603471
Hyperornithinemia-Hyperammonemia-Homocitrullinuria (HHH) Syndrome	*SLC25A15*	AR \ 238970
Carnitine-acylcarnitine translocase deficiency	*SLC25A20*	AR \ 212138
Achondrogenesis, Type 1B	*SLC26A2*	AR \ 600972
Congenital Chloride Diarrhea	*SLC26A3*	AR \ 214700
Pendred Syndrome	*SLC26A4*	AR \ 274600
Autism Spectrum, Epilepsy and Arthrogryposis	*SLC35A3*	AR \ 615553
Glycogen Storage Disease, Type IB	*SLC37A4*	AR \ 232220
Acrodermatitis Enteropathica	*SLC39A4*	AR \ 201100

Oculocutaneous albinism, Type 4	*SLC45A2*	AR \ 606574
Corneal Dystrophy and Perceptive Deafness	*SLC4A11*	AR \ 217400 , 217700
Creatine Transporter Defect (Cerebral Creatine Deficiency Syndrome 1, X-Linked)	*SLC6A8*	XLR \ 300352
Lysinuric Protein Intolerance	*SLC7A7*	AR \ 222700
Cystinuria, Type B	*SLC7A9*	AR \ 220100
Schimke Immunoosseous Dysplasia	*SMARCAL1*	AR \ 242900
Niemann-Pick Disease, Types A/B	*SMPD1*	AR \ 257200, 607616
5-alpha reductase deficiency	*SRD5A2*	AR \ 264600
GM3 synthase deficiency	*ST3GAL5*	AR \ 609056
Lipoid Congenital Adrenal Hyperplasia	*STAR*	AR \ 201710
Mitochondrial DNA depletion syndrome 5 (encephalomyopathic with or without methylmalonic aciduria)	*SUCLA2*	AR \ 612073
Multiple Sulfatase Deficiency	*SUMF1*	AR \ 272200
Leigh Syndrome	*SURF1*	AR \ 220110
Tyrosinemia, Type II	*TAT*	AR \ 276600
Osteopetrosis, Infantile Malignant, TCIRG1-Related	*TCIRG1*	AR \ 259700
Hereditary Spastic Paraparesis, Type 49	*TECPR2*	AR \ 615031
Hemochromatosis, Type 3, TFR2-Related	*TFR2*	AR \ 604250
Lamellar Ichthyosis, Type 1	*TGM1*	AR \ 242300
Segawa Syndrome, TH-Related	*TH*	AR \ 605407
Deafness, autosomal dominant 36, autosomal recessive 7	*TMC1*	AR \ 600974
Joubert Syndrome 2 / Meckel Syndrome 2	*TMEM216*	AR \ 608091, 603194
Congenital hypothyroidism	*TPO*	AR \ 274500
Ceroid Lipofuscinosis, Neuronal, 2	*TPP1*	AR \ 204500
Aicardi-Goutieres syndrome, TREX1-related	*TREX1*	AD,AR \ 225750
Bardet-Biedl syndrome 11	*TRIM32*	AR \ 615988
Mulibrey nanism syndrome	*TRIM37*	AR \ 253250
Acute Infantile Liver Failure, TRMU-Related	*TRMU*	AR \ 613070
Pontocerebellar hypoplasia	*TSEN54*	AR \ 610204, 277470, 225753
Combined Oxidative Phosphorylation Deficiency 3	*TSFM*	AR \ 610505
Congenital hypothyroidism	*TSHB*	AR \ 275100
Hypothyroidism, congenital, nongoitrous, 1	*TSHR*	AR \ 275200
Tricho-Hepato-Enteric Syndrome	*TTC37*	AR \ 222470
Familial dilated cardiomyopathy	*TTN*	AR \ 611705
Ataxia with Vitamin E Deficiency	*TTPA*	AR \ 277460
Myoneurogastrointestinal Encephalopathy (MNGIE)	*TYMP*	AR \ 603041
Oculocutaneous Albinism, Type 1	*TYR*	AR \ 606952
Oculocutaneous albinism, Type 3	*TYRP1*	AR \ 203290
Crigler-Najjar Syndrome	*UGT1A1*	AR \ 218800, 606785
Beta-ureidopropionase deficiency	*UPB1*	AR \ 613161
Usher Syndrome, Type 1C	*USH1C*	AR \ 276904
Cohen Syndrome	*VPS13B*	AR \ 216550

Congenital Neutropenia, VPS45-Related	*VPS45*	AR \ 615285
Pontocerebellar Hypoplasia, Type 2E	*VPS53*	AR \ 615851
Pontocerebellar Hypoplasia, Type 1A	*VRK1*	AR \ 607596
Microphthalmia/Anophthalmia, VSX2-Related	*VSX2*	AR \ 610093 , 610092
Von Willebrand disease	*VWF*	AD,AR \ 277480, 613554
Wiskott-Aldrich syndrome, X-Linked	*WAS*	XLR \ 301000
Progressive Pseudorheumatoid Dysplasia	*WISP3*	AR \ 208230
Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome	*WNT10A*	AR \ 257980
Werner Syndrome	*WRN*	AR \ 277700
Xeroderma pigmentosum Group A	*XPA*	AR \ 278700
Xeroderma Pigmentosum Group C	*XPC*	AR \ 278720
Spastic Paraplegia Type 15	*ZFYVE26*	AR \ 270700