Cincinnati's Undiagnosed and Rare Liver Disease (CURL) Panel

Description:

Inherited liver diseases can manifest with a range of clinical phenotypes, including defects in bile acid synthesis, cholestasis, hepatosplenomegaly, and jaundice. Cholestatic jaundice affects approximately one in every 2,500 full-term infants, with inherited conditions accounting for 25-50% of pediatric cholestasis cases (Fawaz, et al. 2017; Jeyaraj et al. 2021).

These hepatic conditions are attributed to genetic variations in a diverse array of genes and may follow different inheritance patterns such as autosomal dominant, autosomal recessive, or X-linked inheritance. The identification of a genetic etiology for liver disease plays a critical role in promoting early diagnosis and providing tailored medical management, thereby optimizing patient care (Goldberg et al. 2020).

Cincinnati's Undiagnosed and Rare Liver Disease (CURL) Panel employs Exome Sequencing technology in conjunction with phenotype-driven analysis. This panel focuses on a predefined list of 1,447 genes associated with hereditary liver disease. Notably, this CURL panel is currently the most comprehensive gene panel available for diagnosing genetic liver diseases (as of 2023).

Importantly, the CURL panel utilizes the clinical phenotype of patients as guides, ensuring a more precise and patient-specific diagnostic process. Additionally, this testing protocol allows ordering physicians to consult with specialists in pediatric hepatology at Cincinnati Children's Hospital Medical Center, fostering interdisciplinary collaboration and enhancing patient care.

This comprehensive gene list included in the CURL panel was curated through meticulous review of existing literature. We highly recommend utilizing this test as a trio involving the proband and both biological parents, as it enhances the diagnostic yield. Duo and proband-only testing options are also available to accommodate varying circum-stances.

Indications:

- Cholestasis of unknown etiology
- Chronic and fibrogenic hepatitis with unknown etiology
- Personal and family history of cirrhosis with unknown etiology

What is Reported:

Pathogenic and likely pathogenic variants in genes suspected to contribute to the patient's phenotype will be reported. Variants of uncertain significance may be reported based on how well it fits with the patient's phenotype. Some variants of uncertain significance may be reported in candidate genes that do not yet have a definitive association with human disease. A list of identified variants of uncertain significance can be provided upon provider request.

What is Not Reported:

Variants that are benign or likely benign will not be reported. Uncommonly, this test may reveal an incidental finding that is not directly related to the test indication. The lack of reported incidental findings for any particular gene does not rule out the possibility of pathogenic variants in that gene.

Methodology:

The CURL Panel uses the Human Comprehensive Exome kit from Twist Bioscience to capture the exonic regions of genes from the genomic DNA.

Cincinnati Children's
changing the outcome together

Genetics and Genomics Diagnostic Laboratory
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www.cincinnatichildrens.org/genetics

Targeted regions are sequenced using an Illumina sequencing system with paired-end reads. Sequence reads are aligned to the human reference genome (GRCh37/hg19 Build). Variants within exons and flanking sequences are identified and evaluated by a validated in-house developed bioinformatics analysis pipeline that includes the usage of GATK and Fabric Genomic Analysis platform. Data quality is assessed to confirm it has a minimum coverage of 20X for >95% of targets of interest.

Technical Limitations:

- Pathogenic variants may be present in a portion of the genes not covered by this test or in regions with suboptimal data due to homologous issue, polynucleotides, or nucleotide repeats, and therefore may not be identified. Thus, the absence of identified pathogenic variants does not exclude the possibility of a genetic etiology for the patient's symptoms.

- Certain types of mutations are not detected. Only single base pair changes or small insertions or deletions of DNA are detected. Large deletions, duplications, or rearrangements, mitochondrial genome mutations, repeat expansions, low level mosaicism and many epigenetic defects may not be detected by this test.

Regions of Homology:

These gene regions with homology may generate suboptimal data with potential false negative results.

Gene	Transcript	Exon	Chrom	Exon_Start	Exon_End
ABCC6	NM_001171	8	16	16297266	16297470
ABCC6	NM_001171	7	16	16302584	16302716
ABCC6	NM_001171	6	16	16306041	16306103
ABCC6	NM_001171	5	16	16308180	16308306
ABCC6	NM_001171	4	16	16313410	16313539
ABCC6	NM_001171	3	16	16313678	16313804
ABCC6	NM_001079528	2	16	16315424	16315688
ABCC6	NM_001171	2	16	16315505	16315688
ABCC6	NM_001171	1	16	16317255	16317291
ALG1	NM_019109	8	16	5129064	5129103
ALG1	NM_019109	13	16	5134750	5134882
AP1B1	NM_001127	3	22	29758989	29759095
AP1B1	NM_001127	2	22	29763195	29763232
ATAD3A	NM_001170535	1	1	1447648	1447853
ATAD3A	NM_001170535	3	1	1452690	1452792
ATAD3A	NM_001170535	4	1	1453095	1453155
ATAD3A	NM_001170535	5	1	1454300	1454370
ATAD3A	NM_001170535	7	1	1455927	1455997
ATAD3A	NM_001170535	11	1	1459652	1459777
ATAD3A	NM_001170535	13	1	1461840	1461911
ATAD3A	NM_001170535	15	1	1464602	1464711
BCR	NM_004327	17	22	23651610	23651670
BCR	NM_004327	18	22	23652510	23652620
BCR	NM_004327	20	22	23655073	23655208
BMPR1A	NM_004329	13	10	88683350	88683476
CA5A	NM_001739	4	16	87936030	87936126
CA5A	NM_001739	3	16	87938391	87938510
CEL	NM_001807	1	9	135937380	135937455
CEL	NM_001807	8	9	135944058	135944245
CEL	NM_001807	9	9	135944442	135944646
CFHR1	NM_002113	1	1	196788974	196789032
CFHR3	NM_021023	4	1	196757345	196757528
CFHR3	NM_021023	5	1	196759174	196759357
CHEK2	NM_007194	15	22	29083884	29083974
CHEK2	NM_007194	14	22	29085122	29085203
CHEK2	NM_007194	13	22	29090019	29090105
CHEK2	NM_007194	12	22	29091114	29091230
COX10	NM_001303	6	17	14095305	14095538
CYP11B2	NM_000498	7	8	143994222	143994301
DUOX2	NM_014080	7	15	45403308	45403475
EFL1	NM_024580	7	15	82530647	82530862
EIF4H	NM_022170	7	7	73609498	73609638
FANCD2	NM_033084	14	3	10085512	10085548
FANCD2	NM_033084	17	3	10091057	10091189
FANCD2	NM_033084	22	3	10106039	10106113
FCGR2A	NM_021642	7	1	161487764	161487938
FKBP6	NM_001135211	2	7	72742275	72742317
FKBP6	NM_003602	2	7	72742431	72742488
FKBP6	NM_003602	3	7	72742577	72742695
FLNC	NM_001458	47	7	128498061	128498271
GBA1	NM_000157	11	1	155204785	155204891
GBA1	NM_000157	5	1	155208307	155208441

Gene	Transcript	Exon	Chrom	Exon_Start	Exon_End
GK	NM_000167	19	X	30746848	30746859
HYDIN	NM_001270974	84	16	70852244	70852475
HYDIN	NM_001270974	83	16	70861163	70861314
HYDIN	NM_001270974	82	16	70862168	70862332
HYDIN	NM_001270974	81	16	70863520	70863733
HYDIN	NM_001270974	79	16	70867789	70868067
HYDIN	NM_001270974	78	16	70869578	70869737
HYDIN	NM_001270974	77	16	70871592	70871791
HYDIN	NM_001270974	76	16	70873966	70874136
IDS	NM_000202	3	X	148584841	148585019
LEFTY2	NM_001172425	3	1	226127455	226127571
LEPR	NM_001003680	20	1	66095884	66096088
MST1	NM_020998	16	3	49721982	49722089
MST1	NM_020998	14	3	49722444	49722522
MST1	NM_020998	13	3	49722694	49722815
MST1	NM_020998	8	3	49723745	49723914
MST1	NM_020998	7	3	49724116	49724235
MST1	NM_020998	6	3	49724379	49724500
MST1	NM_020998	4	3	49724796	49724911
MST1	NM_020998	1	3	49726030	49726124
NOTCH2	NM_024408	4	1	120539619	120539955
NOTCH2	NM_024408	3	1	120547951	120548211
NOTCH2	NM_024408	2	1	120572528	120572610
OCLN	NM_002538	6	5	68840730	68840946
OCLN	NM_002538	7	5	68843756	68843928
OCLN	NM_002538	8	5	68847370	68847412
OCLN	NM_002538	9	5	68849396	68849498
ODAD2	NM_018076	9	10	28257851	28257947
PGK1	NM_000291	11	X	77381286	77381327
PIK3CA	NM_006218	13	3	178937736	178937840
PLEKHM1	NM_014798	9	17	43522835	43523029
PLEKHM1	NM_014798	8	17	43527983	43528129
PLEKHM1	NM_014798	2	17	43559802	43559850
PMS2	NM_000535	15	7	6013029	6013173
PMS2	NM_000535	14	7	6017218	6017388
PMS2	NM_000535	13	7	6018226	6018327
PMS2	NM_000535	2	7	6045522	6045662
RBM8A	NM_005105	6	1	145509165	145509211
RPSA	NM_002295	4	3	39452244	39452490
RPSA	NM_002295	7	3	39453764	39453859
SAA1	NM_000331	2	11	18288434	18288525
SAA1	NM_000331	3	11	18290741	18290880
SDHA	NM_004168	14	5	254507	254621
SDHC	NM_001278172	4	1	161332118	161332330
SDHD	NM_003002	4	11	111965528	111965694
SLC2A3	NM_006931	8	12	8077005	8077107
TMEM231	NM_001077416	3	16	75579249	75579393
TMEM231	NM_001077416	2	16	75579723	75579852
TPI1	NM_000365	7	12	6979428	6979547
ABCC6	NM_001171	2	16	16315505	16315688
ABCC6	NM_001171	1	16	16317255	16317291
ALG1	NM_019109	8	16	5129064	5129103

Low Coverage (<20X) Regions:

These regions represent the low coverage (<20X) regions identified during our test validation. For specific patient cases, these regions may vary.

Gene	Transcript	Exon	Chrom	Exon_Start	Exon_End
ADAMTS9	NM_182920.1	39	3	64507843	64507846
ALG13	NM_001099922.2	5	X	110952185	110952284
ALG8	NM_001007027.2	26	11	77813932	77814002
ANKS6	NM_173551.3	1	9	101558732	101558781
ATP11C	NM_173694.4	57	X	138820200	138820236
ATP11C	NM_173694.4	33	X	138899014	138899031
ATP11C	NM_173694.4	33	X	138899084	138899110
ATP11C	NM_173694.4	58	X	138813805	138813812
ATP11C	NM_173694.4	58	X	138813870	138813871
ATP11C	NM_173694.4	58	X	138813873	138813922
ATP11C	NM_173694.4	31	X	138908855	138908858
ATP7A	NM_000052.5	3	X	77243730	77243732
ATRX	NM_000489.3	68	X	76776258	76776265
BCR	NM_004327.3	18	22	23652503	23652510
CASZ1	NM_001079843.2	37	1	10698991	10699047
CC2D2A	NM_001164720.1	5	4	15482813	15482917
CCNQ	NM_152274.4	6	X	152864496	152864537
CD55	NM_001114752.1	10	1	207513728	207513800
CFH	NM_000186.3	10	1	196682857	196682872
CFHR1	NM_002113.2	4	1	196797197	196797384
CFHR3	NM_021023.5	6	1	196762439	196762441
CORIN	NM_006587.3	50	4	47644050	47644053
CORIN	NM_006587.3	50	4	47644056	47644062
CORIN	NM_006587.3	50	4	47644068	47644074
CTBP1	NM_001328.2	11	4	1242696	1242727
CTBP1	NM_001328.2	11	4	1242750	1242751

Gene	Transcript	Exon	Chrom	Exon_Start	Exon_End
CYBB	NM_000397.3	13	X	37670040	37670048
DNAH8	NM_001206927.1	23	6	38773359	38773380
ENPP1	NM_006208.2	1	6	132129168	132129194
EVC	NM_153717.2	1	4	5713139	5713289
GABRD	NM_000815.4	1	1	1950934	1950936
GPC3	NM_004484.3	28	X	132833915	132833922
GPC4	NM_001448.2	3	X	132458553	132458572
HGSNAT	NM_152419.2	1	8	42995632	42995657
HGSNAT	NM_152419.2	1	8	42995762	42995765
IFT81	NM_031473.3	12	12	110605668	110605791
IL12RB1	NM_153701.1	27	19	18182011	18182151
IQSEC2	NM_001111125.2	32	X	53263492	53263612
ITCH	NM_001257137.1	7	20	33004915	33004932
ITCH	NM_001257137.1	7	20	33004963	33004983
ITCH	NM_001257137.1	7	20	33004985	33005053
JAM2	NM_001270408.1	10	21	27086535	27086625
KIAA0586	NM_001244189.1	33	14	59010593	59010693
KIAA0586	NM_001244189.1	6	14	58907931	58908069
LEPR	NM_001003680.3	20	1	66095877	66096096
LYRM4	NM_001164840.1	10	6	5187021	5187222
MECP2	NM_001110792.1	5	X	153363129	153363130
MTM1	NM_000252.2	5	X	149783177	149783180
MTO1	NM_133645.2	7	6	74190089	74190098
MTO1	NM_001123226.1	8	6	74190726	74190847
NDUFB11	NM_019056.6	4	X	47003864	47003866
OCRL	NM_000276.3	9	X	128694519	128694528
OCRL	NM_000276.3	9	X	128694627	128694636
PHEX	NM_000444.4	14	X	22196382	22196501
PHEX	NM_000444.4	7	X	22112093	22112128
PHKA2	NM_000292.2	21	X	18927054	18927060
RAD51	NM_133487.3	4	15	40993996	40994132
RPGR	NM_001034853.1	34	X	38145323	38145419
RPGR	NM_001034853.1	34	X	38145728	38145758
RPGRIP1L	NM_015272.2	48	16	53656123	53656150
SDHD	NM_001276506.1	4	11	111963796	111963929
SHANK3	NM_033517.1	1	22	51113062	51113070
SHANK3	NM_033517.1	11	22	51135977	51136000
SLC39A8	NM_001135148.1	29	4	103245399	103245432
STOX1	NM_152709.4	1	10	70587659	70587698
TBX1	NM_005992.1	3	22	19748482	19748602
TCTN1	NM_001173976.1	2	12	111054110	111054165
TCTN1	NM_024549.5	6	12	111072193	111072276
TK2	NM_001271934.1	68	16	66581866	66581890
TKT	NM_001258028.1	48	3	53271805	53271844
TSFM	NM_001172696.1	5	12	58185740	58185818
USP9X	NM_001039591.2	18	X	41027454	41027455
USP9X	NM_001039591.2	18	X	41027461	41027474
USP9X	NM_001039591.2	18	X	41027477	41027479
VPS45	NM_001279353.1	13	1	150115008	150115117

Note: CURL Panel cases with negative or uncertain findings can be reflexed to Whole Exome Sequencing (WES). Including biological parental samples is strongly encouraged to assist with the analysis of WES and to increase test yield. Reflex to WES orders can either be placed simultaneously or separately.

Turn-Around Time:

84 days (12 weeks)

Specimen:

At least 3 mls whole blood in a lavender top (EDTA) tube or saliva in an Oragene saliva kit. Please call 513-636-4474 for a free saliva collection kit. Label the tube with the patient's name, birth date, and date of collection. Alternatively, 10 mcg of high quality DNA extracted in a CLIA certified lab may be submitted.

CPT Codes:

Cincinnati's Undiagnosed and Rare Liver Disease (CURL) Panel:

- Trio (proband and two family members): **81403, 81404, 81406(x2), 81479(x3)**
- Additional family members: **81479**
- Proband only: **81403, 81404, 81406(x2), 81479**

Shipping Instructions:

Please enclose **test requisition** with sample. **All information must be completed before sample can be processed.**

Place samples in Styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Saturday.

Ship to:

Genetics and Genomics Diagnostic Laboratory
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229
513-636-4474

References:

Almes M, et al. (2022). Targeted-Capture Next-Generation Sequencing in Diagnosis Approach of Pediatric Cholestasis. Diagnostics (Basel). 12(5):1169.

Amer S, et al. (2014). A Comprehensive Review of Progressive Familial Intrahepatic Cholestasis (PFIC): Genetic Disorders of Hepatocanalicular Transporters. Gastroenterology Res. 7(2):39-43.

Berauer JP, et al. (2019). Identification of Polycystic Kidney Disease 1 Like 1 Gene Variants in Children With Biliary Atresia Splenic Malformation Syndrome. Hepatology. 70(3):899-910.

Fawaz R, et al. (2017). Guideline for the Evaluation of Cholestatic Jaundice in Infants: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr. 64(1):154-168.

Goldberg A & Mack CL. (2020). Inherited Cholestatic Diseases in the Era of Personalized Medicine. Clin Liver Dis (Hoboken). 15(3):105-109.

Jeyaraj R, et al. (2021). The Genetics of Inherited Cholestatic Disorders in Neonates and Infants: Evolving Challenges. Genes (Basel). 12(11):1837.

Lam, WY, et al. (2021). Identification of a wide spectrum of ciliary gene mutations in nonsyndromic biliary atresia patients implicates ciliary dysfunction as a novel disease mechanism. EBioMedicine, 71:103530.

See pages **6-8** for a complete list of genes sequenced on the CURL Panel

Gene List (1,447 Genes):

A2ML1, ABCA1, ABCA2, ABCB11, ABCB4, ABCC12, ABCC2, ABCC6, ABCC8, ABCD1, ABCD3, ABCG5, ABCG8, ABHD5, ABL1, ACAD8, ACAD9, ACADM, ACADS, ACADVL, ACAT1, ACAT2, ACOX1, ACOX2, ACP5, ACTG2, ACTN4, ACVR2B, ACVRL1, ADA, ADA2 (CECR1), ADAMTS13, ADAMTS3, ADAMTS9, ADAMTSL2, ADAR, ADCY3, ADK, AEBP1, AGA, AGGF1, AGL, AGPAT2, AGXT, AHCY, AHI1, AIFM1, AIRE, AK7, AKR1D1, AKT1, AKT2, ALAS2, ALB, ALDH6A1, ALDOA, ALDOB, ALG1, ALG12, ALG13, ALG2, ALG3, ALG6, ALG8, ALG9, ALMS1, ALPK1, AMACR, ANGPTL3, ANK1, ANKRD55, ANKS6, ANTXR1, AP1B1, AP1S1, AP3B1, AP3D1, APC, APC2, APOA1, APOA2, APOA5, APOB, APOC2, APOC3, APOE, APPL1, APTX, AR, ARG1, ARHGAP31, ARID1A, ARID1B, ARID2, ARL13B, ARL3, ARL6, ARMC9, ARSA, ARSB, ARVCF, ASAH1, ASL, ASS1, ASXL1, ATAD3A, ATM, ATP11C, ATP5F1E (ATP5E), ATP6AP1, ATP6AP2, ATP6V0A4, ATP6V1B1, ATP6V1B2, ATP7A, ATP7B, ATP8B1, ATPAF2, ATRX, ATXN10, AUH, AXIN1, B2M, B3GLCT (B3GALTL), B9D1, B9D2, BAAT, BACH2, BAP1, BAZ1B, BBIP1, BBS1, BBS10, BBS12, BBS2, BBS4, BBS5, BBS7, BBS9, BCHE, BCL2, BCL6, BCO1 (BCMO1), BCR, BCS1L, BICC1, BLK, BLNK, BLVRA, BMP2, BMPER, BMPR1A, BOLA3, BPGM, BRAF, BRCA1, BRCA2, BRIP1, BSCL2, BTD, BTK, BTNL2, BUD23 (WBSCR22), C1QBP, C1S, C2CD3, C2ORF69, CA2, CA5A, CACNA1S, CAD, CALR, CARD11, CARS2, CASK, CASP10, CASP8, CASR, CASZ1, CAV1, CAV3, CAVIN1 (PTRF), CBL, CBS, CC2D2A, CCBE1, CCDC103, CCDC115, CCDC28B, CCDC32 (C15orf57), CCDC39, CCDC40, CCDC47, CCDC65, CCND1, CCNO, CCNQ (FAM58A), CCT5, CD19, CD247, CD27, CD28, CD3D, CD3E, CD40LG, CD55, CD70, CD79A, CD79B, CD81, CD96, CDAN1, CDC73, CDKN1B, CDKN1C, CDKN2A, CDON, CEACAM6, CEL, CELSR2, CENPF, CEP104, CEP120, CEP164, CEP19, CEP290, CEP41, CEP55, CEP83 (CCDC41), CETP, CFAP221, CFAP298 (C21orf59), CFAP300 (C11orf70), CFAP410 (C21orf2), CFAP418 (C8orf37), CFAP53 (CCDC11), CFAP57 (WDR65), CFH, CFHR1, CFHR3, CFTR, CHD7, CHEK2, CIDEC, CIITA, CILK1 (ICK), CLCA4, CLCN7, CLDN1, CLDN16, CLEC7A, CLIP2, CLPB, CLUAP1, CNOT1, COA3, COA6, COA8 (APOPT1), COG1, COG2, COG4, COG5, COG6, COG7, COG8, COL7A1, COMT, COQ2, CORIN, COX10, COX14, COX15, COX16, COX20, COX4I1, COX4I2, COX5A, COX6A2, COX6B1, CP, CPA1, CPE, CPLANE1 (C5orf42), CPLX1, CPOX, CPS1, CPT1A, CPT2, CR2, CRB2, CREB3L3, CRELD1, CSPP1, CTBP1, CTC1, CTCF, CTLA4, CTNNB1, CTNS, CTRC, CTSA, CTSC, CTSK, CTU2, CUL3, CYBA, CYBB, CYBC1 (C17orf62), CYC1, CYP11A1, CYP11B2, CYP19A1, CYP27A1, CYP27B1, CYP2R1, CYP3A4, CYP7A1, CYP7B1, D2HGDH, DAAM2, DAXX, DCAF17, DCDC2, DCLRE1C, DCTN4, DDOST, DDRGK1, DDX59, DEAF1, DGAT1, DGUOK, DHCR24, DHCR7, DHDDS, DHFR, DIS3L2, DISP1, DKC1, DLAT, DLD, DLK1, DLL4, DMP1, DMPK, DNAAF1, DNAAF11 (LRRC6), DNAAF2, DNAAF3, DNAAF4 (DYX1C1), DNAAF5 (HEATR2), DNAAF6 (PIH1D3), DNAH1, DNAH11, DNAH5, DNAH6, DNAH8, DNAH9, DNAI1, DNAI2, DNAJB11, DNAJB13, DNAJC19, DNAJC21, DNAJC30, DNAL1, DNASE1L3, DOCK6, DOLK, DPAGT1, DPF2, DPM1, DPM2, DPM3, DPYS, DRC1, DUOX2, DUOXA2, DYNC2H1, DYNC2I1 (WDR60), DYNC2I2 (WDR34), DYNC2LI1, DYNLT2B (TCTEX1D2), DYRK1B, DZIP1L, EARS2, EBP, ECHS1, EDNRA, EFL1 (EFTUD1), EHHADH, EIF2AK3, EIF4H, ELMO2, ELN, EMD, ENG, ENPP1, EOGT, EPB41, EPB42, EPCAM, EPG5, EPHX1, EPHX2, EPM2A, ERAP1, ERBB3, ERCC1, ERCC4, ERCC6, ERCC8, ESCO2, ESR1, ETFA, ETFB, ETFDH, EVC, EVC2, EWSR1, EXOC2, EXOC3L2, EXOC8, EXTL3, EYA1, F13A1, F13B, F5, FADD, FAH, FAM111A, FAM111B, FAM149B1, FAM20C, FAN1, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FARSA, FARSB, FAS, FASLG, FAT4, FBN1, FBP1, FBXL4, FCGR2A, FCGR3B, FCHO1, FDFT1, FDX2 (FDX1L), FECH, FERMT3, FGA, FGB, FGF23, FGF8, FGFR1, FGFR2, FGFR3, FGFRL1, FGG, FH, FHL1, FKBP10, FKBP6, FLCN, FLI1, FLII, FLNC, FLT1, FMO3, FN1, FOS, FOXF1, FOXH1, FOXJ1, FOXP3, FOXRED1, FUCA1, G6PC1 (G6PC), G6PC3, G6PD, GAA, GABRD, GALE, GALK1, GALM, GALNS, GALNT2, GALT, GANAB, GAS2L2, GAS8, GATA1, GATA2, GATA3, GATA4, GATA6, GATC, GATM, GBA1 (GBA), GBE1, GCDH, GCGR, GCK, GCLC, GDF1, GDF2, GFER, GFM1, GHR, GK, GLA, GLB1, GLI2, GLI3, GLIS2, GLIS3, GLRX5, GLYCTK, GM2A, GNAS, GNE, GNMT, GNPTAB, GNS, GP1BA, GP1BB, GPBAR1, GPC3, GPC4, GPD1, GPI, GPIHBP1, GPR35, GPX1, GRHPR, GSN, GSR, GSS, GSTM3, GTPBP3, GUCY2D, GUSB, GYPC, GYS2, HADH, HADHA, HADHB, HAMP, HAVCR2, HESX1, HEXA, HEXB, HFE, HGSNAT, HIBCH, HIRA, HJV (HFE2), HK1, HLCS, HMBS, HMGA2, HMGCL, HMGCS2, HMOX1, HNF1A, HNF1B, HNF4A, HNRNPA1, HNRNPA2B1, HOGA1, HOXD13, HPD, HPGD, HSD17B10, HSD17B4, HSD3B7, HSPG2, HTT, HYDIN, HYLS1, HYOU1,

IARS1 (IARS), IBA57, ICOS, IDS, IDUA, IER3IP1, IFIH1, IFNG, IFNGR1, IFT122, IFT140, IFT172, IFT27, IFT43, IFT52, IFT57, IFT74, IFT80, IFT81, IGF1, IGF2, IGF2R, IGHM, IKZF1, IKZF3, IL10, IL12A, IL12RB1, IL17F, IL17RA, IL17RC, IL18BP, IL1RN, IL21R, IL23R, IL2RA, IL2RB, IL2RG, IL36RN, IL6, IL7R, INPP5E, INPPL1, INS, INSR, INTU, INVS, IQCB1, IQSEC2, IRAK4, IRF5, IRF8, ISCU, ITCH, ITK, IVD, IYD, JAG1, JAK1, JAK2, JAK3, JAM2, JAM3, JMJD1C, KARS1 (KARS), KATNIP, KCNAB2, KCNH1, KCNJ1, KCNJ11, KCNJ5, KCNN3, KCNN4, KCNQ1, KDM3B, KDM5C, KIAA0586, KIAA0753, KIF12, KIF14, KIF20A, KIF23, KIF3B, KIF7, KIT, KLF1, KLF11, KLHL3, KLRC4, KMT2E, KPTN, KRAS, KRIT1, KRT18, KRT8, KYNU, LACC1, LARS1 (LARS), LARS2, LAT, LBR, LCAT, LCT, LDHA, LDLR, LDLRAP1, LEFTY2, LEMD3, LEP, LEPR, LETM1, LHX3, LHX4, LIG4, LIMK1, LIPA, LIPC, LIPE, LIPT1, LIPT2, LMAN1, LMBRD1, LMF1, LMNA, LMNB2, LONP1, LPIN2, LPL, LRBA, LRP5, LRP6, LRPPRC, LRRC56, LRRC8A, LRRCC1, LTBP3, LTC4S, LUZP1, LYRM4, LYST, LYZ, LZTFL1, LZTR1, MAD2L2, MADD, MAGT1, MAN2B1, MAPKBP1, MARS1 (MARS), MC4R, MCCC1, MCCC2, MCEE, MCFD2, MCIDAS, MCM10, MCM4, MCOLN1, MECP2, MED12, MED13L, MED25, MEF2A, MEFV, MEGF8, MET, METTL27 (WBSCR27), MFN2, MICOS13 (C19orf70), MIEF2, MIF, MKKS, MKS1, MLH1, MLH3, MLXIPL, MLYCD, MMAA, MMAB, MMACHC, MMEL1, MMP1, MMP15, MMP21, MMUT (MUT), MNS1, MOGS, MPC1, MPI, MPIG6B (C6orf25), MPL, MPV17, MRAS, MRE11 (MRE11A), MRM2 (FTSJ2), MRPL12, MRPL3, MRPL44, MRPS14, MRPS22, MRPS23, MRPS25,MRPS28, MRPS7, MS4A1, MSH2, MSH6, MSMO1, MST1, MTFMT, MTM1, MTO1, MTRR, MTTP, MTX2, MUC5B, MVK, MYBPC3, MYC, MYCN, MYD88, MYO5A, MYO5B, MYORG (KIAA1161), MYPN, MYRF, NAB2, NADK2, NAGA, NAGLU, NAGS, NBAS, NBEAL2, NCF2, NCF4, NCKAP1L, NDUFA1, NDUFA10, NDUFA11, NDUFA12, NDUFA13, NDUFA2, NDUFA4, NDUFA6, NDUFA8, NDUFA9, NDUFAF1, NDUFAF2, NDUFAF3, NDUFAF4, NDUFAF5, NDUFAF6, NDUFAF8 (C17orf89), NDUFB10, NDUFB11, NDUFB3, NDUFB8, NDUFB9, NDUFC2, NDUFS1, NDUFS2, NDUFS3, NDUFS4, NDUFS6, NDUFS7, NDUFS8, NDUFV1, NDUFV2, NEK1, NEK10, NEK8, NELFA, NEU1, NEUROD1, NEUROG3, NFKB1, NFKB2, NFS1, NFU1, NGLY1, NHLRC1, NHLRC2, NHP2, NKX2-5, NLRC4, NLRP1, NLRP12, NLRP3, NME8, NOD2, NODAL, NOP10, NOTCH1, NOTCH2, NPC1, NPC2, NPHP1, NPHP3, NPHP4, NPHS1, NPHS2, NPM1, NR1H4, NR2F2, NR3C2, NRAS, NSD1, NSD2 (WHSC1), NSDHL, NSMCE2, NUBPL, NUP107, OCLN, OCRL, ODAD1 (CCDC114), ODAD2 (ARMC4), ODAD3 (CCDC151), ODAD4 (TTC25), ODC1, OFD1, OGDH, ORAI1, OSTM1, OTC, OTUD5, P4HA2, PAFAH1B1, PALB2, PALLD, PANK2, PARN, PARS2, PAX4, PAX8, PC, PCCA, PCCB, PCK1, PCK2, PCSK1, PCSK9, PCYT1A, PDE6D, PDGFB, PDGFRA, PDGFRB, PDGFRL, PDHA1, PDHB, PDHX, PDP1, PDPN, PDSS2, PDX1, PEPD, PET100, PET117, PEX1, PEX10, PEX11B, PEX12, PEX13, PEX14, PEX16, PEX19, PEX2, PEX26, PEX3, PEX5, PEX6, PEX7, PFKM, PGAP2, PGAP3, PGK1, PGM1, PHEX, PHGDH, PHKA2, PHKB, PHKG2, PHYH, PIBF1, PIEZO1, PIGA, PIGB, PIGG, PIGH, PIGL, PIGM, PIGO, PIGQ, PIGS, PIGT, PIGV, PIGW, PIGY, PIK3C2A, PIK3CA, PIK3CD, PIK3R1, PIK3R5, PITRM1, PKD1L1, PKD2, PKHD1, PKLR, PLA2G4A, PLA2G7, PLAGL1, PLEC, PLEKHM1, PLIN1, PLPBP (PROSC), PLVAP, PMM2, PMS1, PMS2, PNLIP, PNP, PNPLA2, PNPLA6, PNPLA8, PNPO, PNPT1, POC1B, POLD1, POLG, POLG2, POLR3A, POMC, PORCN, POU1F1, POU2AF1, POU6F2, PPA2, PPARG, PPM1B, PPM1F, PPOX, PPP1R17, PPP1R21, PRDM16, PRDX1, PREPL, PRF1, PRKAR1A, PRKCD, PRKCSH, PROP1, PRPS1, PRSS1, PSAP, PSAT1, PSMB10, PSMB4, PSMB8, PSMB9, PSMG2, PSPH, PSTPIP1, PTCD3, PTEN, PTGS1, PTH1R, PTPN11, PTPN2, PTPN22, PTPN3, PTPRC, PTRH2, PYGL, QRSL1, RAB23, RAB27A, RABL3, RAC2, RAD51, RAD51C, RAF1, RAG1, RAG2, RAI1, RARB, RASA2, RASGRP1, RB1, RBCK1, RBM8A, RBPJ, RECQL4, RELA, RELN, RERE, REST, RFC2, RFT1, RFWD3, RFX5, RFX6, RFXANK, RFXAP, RHAG, RHBDF2, RINT1, RIPK1, RIT1, RMND1, RNASEH2A, RNASEH2B, RNASEH2C, RNF43, RPGR, RPGRIP1, RPGRIP1L, RPS20, RPSA, RRAS, RRAS2, RREB1, RRM2B, RSPH1, RSPH3, RSPH4A, RSPH9, RSPO1, RTEL1, RTL1, RUNX1, RYR1, SAA1, SAMD9, SAMD9L, SAMHD1, SAR1B, SBDS, SC5D, SCAPER, SCARB2, SCLT1, SCNN1A, SCNN1B, SCNN1G, SCO1, SCO2, SCP2, SCYL1, SDCCAG8, SDHA, SDHB, SDHC, SDHD, SEC23B, SEC63, SEMA4A, SEMA4D, SEMA7A, SERPINA1, SERPINC1, SETBP1, SETD2, SETX, SF3B1, SFTPC, SGMS2, SGPL1, SGSH, SH2B3, SH2D1A, SHANK3, SHH, SHPK, SIK3, SIX1, SIX3, SKI, SKIC2 (SKIV2L), SKIC3 (TTC37), SLC10A1, SLC10A2, SLC11A1, SLC11A2, SLC12A1, SLC12A3, SLC16A2, SLC17A5, SLC19A1, SLC19A3, SLC20A2, SLC22A5, SLC25A1, SLC25A10, SLC25A13, SLC25A15, SLC25A19, SLC25A20, SLC25A26, SLC25A3, SLC25A4, SLC26A1, SLC26A4, SLC26A9, SLC27A5, SLC29A3, SLC2A1, SLC2A2, SLC2A3, SLC30A10, SLC30A7, SLC34A1, SLC34A2, SLC34A3, SLC35A2, SLC35C1, SLC37A4, SLC39A4, SLC39A8, SLC3A1, SLC40A1, SLC44A1, SLC4A1, SLC4A4, SLC51B, SLC52A1, SLC5A1, SLC5A5, SLC6A14, SLC7A7, SLC9A3, SLCO1B1, SLCO1B3, SLCO2A1, SLX4, SMAD2, SMAD4,

SMARCA4, SMARCAL1, SMARCB1, SMARCC2, SMARCD1, SMARCE1, SMPD1, SNX10, SNX14, SOCS1, SON, SOS1, SOS2, SOST, SOX10, SOX11, SOX4, SP110, SPAG1, SPECC1L, SPEF2, SPEN, SPIB, SPINK1, SPOP, SPRTN, SPTA1, SPTB, SPTBN1, SQSTM1, SRCAP, SRP54, SRSF2, STAR, STAT1, STAT3, STAT4, STAT6, STEAP3, STIL, STIM1, STK11, STK36, STN1 (OBFC1), STOX1, STRA6, STT3B, STX11, STX1A, STX3, STXBP2, SUCLA2, SUCLG1, SUFU, SUGCT, SUMF1, SURF1, SYK, SYNE1, SYNE2, TACO1, TALDO1, TANGO2, TARS2, TBCK, TBL1X, TBL2, TBX1, TBX19, TBXAS1, TCF3, TCF4, TCIRG1, TCTN1, TCTN2, TCTN3, TDP1, TERT, TET2, TF, TFAM, TFG, TFR2, TG, TGFB1, TGFBR2, THPO, TIMM22, TIMM50, TIMMDC1, TINF2, TJP2, TK2, TKFC (DAK), TKT, TLR4, TMEM107, TMEM126B, TMEM138, TMEM165, TMEM199, TMEM216, TMEM231, TMEM237, TMEM270 (WBSCR28), TMEM43, TMEM67, TMEM70, TMPRSS6, TNFRSF11A, TNFRSF11B, TNFRSF13B, TNFRSF13C, TNFRSF1A, TNFRSF1B, TNFRSF4, TNFSF11, TNFSF12, TNFSF15, TNNI3, TNNT2, TNPO3, TOGARAM1 (FAM179B), TP53, TPI1, TPO, TPP2, TRAF3IP1, TRAF3IP2, TRAPPC11, TRAPPC3, TREX1, TRHR, TRIM28, TRIM32, TRIM37, TRIP11, TRIP13, TRMT10C, TRMT5, TRMU, TRNT1, TRPV6, TSC1, TSC2, TSFM, TSHB, TSHR, TTC12, TTC21B, TTC26, TTC7A, TTC8, TTPA, TUFM, TWIST1, TWNK (C10orf2), TXN2, TXNDC15, TYMP, UBAC2, UBE2A, UBE2T, UBE3B, UBE4B, UBR1, UCP2, UFD1 (UFD1L), UGT1A1, UMPS, UNC13D, UNC45A, UQCC2, UQCRB, UQCRC2, UQCRFS1, UROC1, UROD, UROS, USB1, USP9X, VCP, VDR, VHL, VIPAS39, VPS13A, VPS33A, VPS33B, VPS37D, VPS45, VPS4A, VPS50 (CCDC132), VPS51, WDPCP, WDR1, WDR19, WDR35, WNK1, WNK4, WNT3, WRAP53, WT1, XIAP, XK, XPNPEP3, XPR1, XRCC2, XRCC4, XYLT1, YARS1 (YARS), YARS2, ZAP70, ZEB2, ZFYVE19, ZIC2, ZIC3, ZMPSTE24, ZMYND10, ZNF423, ZNF687, ZNF699, ZPR1 (ZNF259)