Blueprint Genetics

Cholestasis Panel

Test code: GA0501

Is a 52 gene panel that includes assessment of non-coding variants.

Is ideal for patients who have any type of cholestasis including those with clinical suspicion of Alagille syndrome, citrullinemia type 2, Crigler-Najjar syndrome types 1 and 2, Dubin-Johnson syndrome, Gilbert syndrome, intrahepatic cholestasis of pregnancy type 3 or progressive familial intrahepatic cholestasis types 1-4.

About Cholestasis

Cholestasis is characterized by jaundice and pruritus. It can present as the hallmark feature in progressive familial intrahepatic cholestasis (PFIC) or as a feature in other inherited disorders such as Alagille syndrome where cholestasis occur in 95% of cases in the neonatal period. PFIC is a group of autosomal recessive liver disorders caused by defects in bile secretion and is characterized by intrahepatic cholestasis with disease onset usually in infancy and childhood. PFIC patients usually develop fibrosis and end-stage liver disease before adulthood. Defects in PFIC-associated genes *ATP8B1* and *ABCB11* may also cause a milder disease called benign recurrent intrahepatic cholestasis. There are several other inherited disorders where cholestasis is frequent such as Alagille syndrome (*JAG1* and *NOTCH2*), arthrogryposis, renal dysfunction, and cholestasis syndrome (ARC syndrome; *VPS33B* and *VIPAS39*), alpha-1-antitrypsin deficiency (*SERPINA1*), citrullinemia (*SLC25A13*), congenital defects of bile acid synthesis (*HSD3B7* and *AKR1D1*), familial hypercholanemia (*TJP2* and *BAAT*) and neonatal ichthyosis-sclerosing cholangitis syndrome (*CLDN1*). The prevalence of PFIC is unknown while the prevalence is as follows for other causes of cholestasis: Dubin-Johnson 1:1,300 in Iranian or Moroccan Jews, Alagille syndrome 1:30,000, Crigler-Najjar syndrome 1:1,000,000. The Gilbert syndrome prevalence is 3-7% but it does cause only abnormal laboratory findings but no clinical symptoms.

Availability

4 weeks

Gene Set Description

Genes in the Cholestasis Panel and their clinical significance

Gene	Associated phenotypes	Inheritance	ClinVar	HGMD
ABCB11	Cholestasis, Cholestasis, benign recurrent intrahepatic, 2	AD/AR	35	299
ABCB4	Gallbladder disease, Low phospholipid-associated cholelithiasis, Cholestasis	AD/AR	27	224
ABCC2	Dubin-Johnson syndrome	AD/AR	29	46
AKR1D1	Bile acid synthesis defect, congenital, 2	AR	7	14
ATP8B1	Intrahepatic cholestasis of pregnancy, Familial intrahepatic cholestasis, recurrent, Cholestasis, progressive familial intrahepatic, Benign recurrent intrahepatic cholestasis	AD/AR	18	131
BAAT	Hypercholanemia, familial	AR	3	7
CFTR	Cystic fibrosis, Congenital bilateral absence of the vas deferens	AD/AR	518	1803
CLDN1	Ichthyosis, leukocyte vacuoles, alopecia, and sclerosing cholangitis	AR	3	4
CREB3L3	Hypertriglyceridaemia	AD		9

CYP7B1	Bile acid synthesis defect, Spastic paraplegia 5A, autosomal recessive	AR	18	60
DCDC2	Deafness, Nephronophthisis, Sclerosing cholangitis, neonatal	AR	13	9
DGUOK	Mitochondrial DNA depletion syndrome, Portal hypertension, noncirrhotic, Progressive external ophthalmoplegia with mitochondrial DNA deletions, autosomal recessive 4	AR	23	62
EPCAM	Diarrhea 5, with tufting enteropathy, congenital, Colorectal cancer, hereditary nonpolyposis	AD/AR	38	80
FAH	Tyrosinemia	AR	53	102
HSD3B7	Bile acid synthesis defect, congenital, 1	AR	8	25
JAG1	Alagille syndrome	AD	131	610
LCT	Lactase deficiency	AR	11	15
LIPA	Wolman disease, Cholesterol ester storage disease	AR	27	93
LMF1	Combined lipase deficiency	AR	4	14
MKS1	Bardet-Biedl syndrome, Meckel syndrome	AR	50	52
MPV17	Mitochondrial DNA depletion syndrome	AR	35	50
MYO5B*	Diarrhea, with microvillus atrophy	AR	14	80
NEUROG3	Diarrhea, malabsorptive, congenital	AR	3	8
NOTCH2*	Alagille syndrome, Hajdu-Cheney syndrome	AD	37	70
NPC1	Niemann-Pick disease	AR	164	472
NPC2	Niemann-pick disease	AR	21	27
NPHP1	Nephronophthisis, Joubert syndrome, Senior-Loken syndrome	AR	19	76
NPHP3	Nephronophthisis, Renal-hepatic-pancreatic dysplasia, Meckel syndrome	AR	38	75
NPHP4	Nephronophthisis, Senior-Loken syndrome	AR	20	113
NR1H4	Cholestasis, progressive familial intrahepatic 5	AR	6	5
PEX1	Heimler syndrome, Peroxisome biogenesis factor disorder 1A, Peroxisome biogenesis factor disorder 1B	AR	112	134
PEX10	Adrenoleukodystrophy, neonatal, Zellweger syndrome, Peroxisome biogenesis disorder, Ataxia	AR	34	29
PEX12	Zellweger syndrome, Peroxisome biogenesis disorder	AR	43	37
PEX2	Zellweger syndrome, Peroxisome biogenesis disorder	AR	16	18
PEX26	Adrenoleukodystrophy, neonatal, Zellweger syndrome, Peroxisome biogenesis disorder	AR	13	27
PEX5	Adrenoleukodystrophy, neonatal, Rhizomelic chondrodysplasia punctata, Zellweger syndrome, Peroxisome biogenesis disorder	AR	8	14

PEX6	Heimler syndrome, Peroxisome biogenesis disorder 4A, Peroxisome biogenesis disorder 4B	AR	58	107
SCYL1	Spinocerebellar ataxia, autosomal recessive 21	AR	12	6
SERPINA1	Alpha-1-antitrypsin deficiency	AR	49	80
SLC25A13	Citrin deficiency	AR	24	113
SLC26A3	Diarrhea, secretory chloride, congenital	AR	55	88
SLCO1B1	Hyperbilirubinemia, Rotor type, digenic	AD/Digenic	3	5
SLCO1B3	Hyperbilirubinemia, Rotor type, digenic	Digenic	2	7
SMPD1	Niemann-Pick disease	AR	110	249
SPINT2	Diarrhea, secretory sodium, congenital	AR	6	12
TJP2	Cholestasis, progressive familial intrahepatic, Hypercholanemia, familial, Deafness, autosomal dominant 51	AD/AR	25	27
TMEM216	Joubert syndrome, Meckel syndrome	AR	17	8
TRMU	Liver failure, infantile, Reversible infantile respiratory chain deficiency	AR	20	21
TTC37	Trichohepatoenteric syndrome, Primary immunodeficiency	AR	12	64
UGT1A1	Crigler-Najjar syndrome, Gilbert syndrome, Breast milk jaundice	AD/AR	29	144
VIPAS39	Arthrogryposis, renal dysfunction, and cholestasis 2	AR	8	13
VPS33B	Arthrogryposis - renal dysfunction - cholestasis	AD/AR	17	58

*

Some, or all, of the gene is duplicated in the genome. Read more.

#

The gene has suboptimal coverage (means <90% of the gene's target nucleotides are covered at >20x with mapping quality score (MQ>20) reads), and/or the gene has exons listed under Test limitations section that are not included in the panel as they are not sufficiently covered with high quality sequence reads.

The sensitivity to detect variants may be limited in genes marked with an asterisk (*) or number sign (#). Due to possible limitations these genes may not be available as single gene tests.

Gene refers to the HGNC approved gene symbol; Inheritance refers to inheritance patterns such as autosomal dominant (AD), autosomal recessive (AR), mitochondrial (mi), X-linked (XL), X-linked dominant (XLD) and X-linked recessive (XLR); ClinVar refers to the number of variants in the gene classified as pathogenic or likely pathogenic in this database (ClinVar); HGMD refers to the number of variants with possible disease association in the gene listed in Human Gene Mutation Database (HGMD). The list of associated, gene specific phenotypes are generated from CGD or Mitomap databases.

Non-coding disease causing variants covered by the panel

Gene	Genomic location HG19	HGVS	RefSeq	RS-number
ABCB11	Chr2:169873328	c.77-19T>A	NM_003742.2	
CFTR	Chr7:117119654	c.-495C>T	NM_000492.3	rs397507565
CFTR	Chr7:117119797		NM_000492.3	
CFTR	Chr7:117119900	c.-249G>C	NM_000492.3	
CFTR	Chr7:117119984	c.-165G>A	NM_000492.3	rs145483167
CFTR	Chr7:117120064	c.-85C>G	NM_000492.3	
CFTR	Chr7:117120115	c.-34C>T	NM_000492.3	rs756314710
CFTR	Chr7:117120325	c.53+124T>C	NM_000492.3	
CFTR	Chr7:117179040	c.870-1113_870-1110delGAAT	NM_000492.3	rs397508809
CFTR	Chr7:117182041	c.1117-26_1117-25delAT	NM_000492.3	rs397508159
CFTR	Chr7:117199500	c.1393-18G>A	NM_000492.3	rs397508199
CFTR	Chr7:117218381	c.1585-9412A>G	NM_000492.3	rs397508229
CFTR	Chr7:117227774	c.1585-19T>C	NM_000492.3	rs778457306
CFTR	Chr7:117227921	c.1679+34G>T	NM_000492.3	rs767901668
CFTR	Chr7:117229521	c.1680-886A>G	NM_000492.3	rs397508266
CFTR	Chr7:117229524	c.1680-883A>G	NM_000492.3	
CFTR	Chr7:117229530	c.1680-877G>T	NM_000492.3	rs397508261
CFTR	Chr7:117243855	c.2908+19G>C	NM_000492.3	rs370683572
CFTR	Chr7:117246713	c.2909-15T>G	NM_000492.3	rs397508455
CFTR	Chr7:117246840	c.2988+33G>T	NM_000492.3	
CFTR	Chr7:117251609	c.3140-26A>G	NM_000492.3	rs76151804
CFTR	Chr7:117251619	c.3140-16T>A	NM_000492.3	rs767232138
CFTR	Chr7:117251624	c.3140-11A>G	NM_000492.3	
CFTR	Chr7:117266272	c.3469-1304C>G	NM_000492.3	
CFTR	Chr7:117267864	c.3717+40A>G	NM_000492.3	rs397508595
CFTR	Chr7:117280015	c.3718-2477C>T	NM_000492.3	rs75039782
CFTR	Chr7:117282680	c.3873+33A>G	NM_000492.3	rs397508622
CFTR	Chr7:117288374	c.3874-4522A>G	NM_000492.3	

CFTR	Chr7:117308395	c.*1233T>A	NM_000492.3	
DGUOK	Chr2:74177650	c.444-62C>A	NM_080916.2	
DGUOK	Chr2:74177701	c.444-11C>G	NM_080916.2	rs536746349
EPCAM	Chr2:47606078	c.556-14A>G	NM_002354.2	rs376155665
JAG1	Chr20:10629767	c.1349-12T>G	NM_000214.2	
MYO5B	Chr18:47365503	c.4852+11A>G	NM_001080467.2	
NPC1	Chr18:21132700	c.1554-1009G>A	NM_000271.4	
NPC1	Chr18:21137182	c.882-28A>G/T	NM_000271.4	
NPC1	Chr18:21137182	c.882-28A>G	NM_000271.4	
NPC1	Chr18:21137182	c.882-28A>T	NM_000271.4	
PEX6	Chr6:42933858	c.2301-15C>G	NM_000287.3	rs267608236
PEX6	Chr6:42933952	c.2300+28G>A	NM_000287.3	rs267608237
SERPINA1	Chr14:94854894	c.-5+2dupT	NM_000295.4	
SERPINA1	Chr14:94854896	c.-5+1G>A	NM_000295.4	rs775786225
SMPD1	Chr11:6415102	c.1341-21_1341-18delAATG	NM_000543.4	rs1312743513
UGT1A1	Chr2:234668848	c.-85_-83dupCAT	NM_000463.2	
UGT1A1	Chr2:234668879	c.-41_-40dupTA	NM_000463.2	rs34983651
VPS33B	Chr15:91550814	c.499-11G>A	NM_018668.3	

Test Strengths

The strengths of this test include:

- CAP accredited laboratory
- CLIA-certified personnel performing clinical testing in a CLIA-certified laboratory
- Powerful sequencing technologies, advanced target enrichment methods and precision bioinformatics pipelines ensure superior analytical performance
- Careful construction of clinically effective and scientifically justified gene panels
- Some of the panels include the whole mitochondrial genome (please see the Panel Content section)
- Our Nucleus online portal providing transparent and easy access to quality and performance data at the patient level
- Our publicly available analytic validation demonstrating complete details of test performance
- ~2,000 non-coding disease causing variants in our clinical grade NGS assay for panels (please see 'Non-coding disease causing variants covered by this panel' in the Panel Content section)
- Our rigorous variant classification scheme
- Our systematic clinical interpretation workflow using proprietary software enabling accurate and traceable processing of NGS data
- Our comprehensive clinical statements

Test Limitations

Genes with partial, or whole gene, segmental duplications in the human genome are marked with an asterisk (*) if they overlap with the UCSC pseudogene regions. The technology may have limited sensitivity to detect variants in genes marked with these symbols (please see the Panel content table above).

This test does not detect the following:

- Complex inversions
- Gene conversions
- Balanced translocations
- Some of the panels include the whole mitochondrial genome but not all (please see the Panel Content section)
- Repeat expansion disorders unless specifically mentioned
- Non-coding variants deeper than ±20 base pairs from exon-intron boundary unless otherwise indicated (please see above Panel Content / non-coding variants covered by the panel).

This test may not reliably detect the following:

- Low level mosaicism in nuclear genes (variant with a minor allele fraction of 14.6% is detected with 90% probability)
- Stretches of mononucleotide repeats
- Low level heteroplasmy in mtDNA (>90% are detected at 5% level)
- Indels larger than 50bp
- Single exon deletions or duplications
- Variants within pseudogene regions/duplicated segments
- Some disease causing variants present in mtDNA are not detectable from blood, thus post-mitotic tissue such as skeletal muscle may be required for establishing molecular diagnosis.

The sensitivity of this test may be reduced if DNA is extracted by a laboratory other than Blueprint Genetics.

For additional information, please refer to the Test performance section and see our Analytic Validation.

Test Performance

The genes on the panel have been carefully selected based on scientific literature, mutation databases and our experience.

Our panels are sectioned from our high-quality, clinical grade NGS assay. Please see our sequencing and detection performance table for details regarding our ability to detect different types of alterations (Table).

Assays have been validated for various sample types including EDTA-blood, isolated DNA (excluding from formalin fixed paraffin embedded tissue), saliva and dry blood spots (filter cards). These sample types were selected in order to maximize the likelihood for high-quality DNA yield. The diagnostic yield varies depending on the assay used, referring healthcare professional, hospital and country. Plus analysis increases the likelihood of finding a genetic diagnosis for your patient, as large deletions and duplications cannot be detected using sequence analysis alone. Blueprint Genetics' Plus Analysis is a combination of both sequencing and deletion/duplication (copy number variant (CNV)) analysis.

The performance metrics listed below are from an initial validation performed at our main laboratory in Finland. The performance metrics of our laboratory in Seattle, WA, are equivalent.

Performance of Blueprint Genetics high-quality, clinical grade NGS sequencing assay for panels.

	Sensitivity % (TP/(TP+FN)	Specificity %
Single nucleotide variants	99.89% (99,153/99,266)	>99.9999%
Insertions, deletions and indels by sequence analysis		

1-10 bps	99.2% (7,745/7,806)	>99.9999%
11-50 bps	99.13% (2,524/2,546)	>99.9999%
Copy number variants (exon level dels/dups)		
1 exon level deletion (heterozygous)	100% (20/20)	NA
1 exon level deletion (homozygous)	100% (5/5)	NA
1 exon level deletion (het or homo)	100% (25/25)	NA
2-7 exon level deletion (het or homo)	100% (44/44)	NA
1-9 exon level duplication (het or homo)	75% (6/8)	NA
Simulated CNV detection		
5 exons level deletion/duplication	98.7%	100.00%
Microdeletion/-duplication sdrs (large CNVs, n=37))		
Size range (0.1-47 Mb)	100% (25/25)	

The performance presented above reached by Blueprint Genetics high-quality, clinical grade NGS sequencing assay with the following coverage metrics

Mean sequencing depth	143X
Nucleotides with >20x sequencing coverage (%)	99.86%

Performance of Blueprint Genetics Mitochondrial Sequencing Assay.

	Sensitivity %	**Specificity %**
ANALYTIC VALIDATION (NA samples; n=4)		
Single nucleotide variants		
Heteroplasmic (45-100%)	100.0% (50/50)	100.0%
Heteroplasmic (35-45%)	100.0% (87/87)	100.0%
Heteroplasmic (25-35%)	100.0% (73/73)	100.0%
Heteroplasmic (15-25%)	100.0% (77/77)	100.0%
Heteroplasmic (10-15%)	100.0% (74/74)	100.0%
Heteroplasmic (5-10%)	100.0% (3/3)	100.0%
Heteroplasmic (<5%)	50.0% (2/4)	100.0%
CLINICAL VALIDATION (n=76 samples)		
All types		

Single nucleotide variants n=2026 SNVs		
Heteroplasmic (45-100%)	100.0% (1940/1940)	100.0%
Heteroplasmic (35-45%)	100.0% (4/4)	100.0%
Heteroplasmic (25-35%)	100.0% (3/3)	100.0%
Heteroplasmic (15-25%)	100.0% (3/3)	100.0%
Heteroplasmic (10-15%)	100.0% (9/9)	100.0%
Heteroplasmic (5-10%)	92.3% (12/13)	99.98%
Heteroplasmic (<5%)	88.9% (48/54)	99.93%
Insertions and deletions by sequence analysis n=40 indels		
Heteroplasmic (45-100%) 1-10bp	100.0% (32/32)	100.0%
Heteroplasmic (5-45%) 1-10bp	100.0% (3/3)	100.0%
Heteroplasmic (<5%) 1-10bp	100.0% (5/5)	99,997%
SIMULATION DATA /(mitomap mutations)		
Insertions, and deletions 1-24 bps by sequence analysis; n=17		
Homoplasmic (100%) 1-24bp	100.0% (17/17)	99.98%
Heteroplasmic (50%)	100.0% (17/17)	99.99%
Heteroplasmic (25%)	100.0% (17/17)	100.0%
Heteroplasmic (20%)	100.0% (17/17)	100.0%
Heteroplasmic (15%)	100.0% (17/17)	100.0%
Heteroplasmic (10%)	94.1% (16/17)	100.0%
Heteroplasmic (5%)	94.1% (16/17)	100.0%
Copy number variants (separate artifical mutations; n=1500)		
Homoplasmic (100%) 500 bp, 1kb, 5 kb	100.0%	100.0%
Heteroplasmic (50%) 500 bp, 1kb, 5 kb	100.0%	100.0%
Heteroplasmic (30%) 500 bp, 1kb, 5 kb	100.0%	100.0%
Heteroplasmic (20%) 500 bp, 1kb, 5 kb	99.7%	100.0%
Heteroplasmic (10%) 500 bp, 1kb, 5 kb	99.0%	100.0%
The performance presented above reached by following coverage metrics at assay level (n=66)		
	Mean of medians	Median of medians
Mean sequencing depth MQ0 (clinical)	18224X	17366X

Nucleotides with >1000x MQ0 sequencing coverage (%) (clinical)	100%
rho zero cell line (=no mtDNA), mean sequencing depth	12X

Bioinformatics

The target region for each gene includes coding exons and ±20 base pairs from the exon-intron boundary. In addition, the panel includes non-coding and regulatory variants if listed above (Non-coding variants covered by the panel). Some regions of the gene(s) may be removed from the panel if specifically mentioned in the 'Test limitations" section above. If the test includes the mitochondrial genome the target region gene list contains the mitochondrial genes. The sequencing data generated in our laboratory is analyzed with our proprietary data analysis and annotation pipeline, integrating state-of-the art algorithms and industry-standard software solutions. Incorporation of rigorous quality control steps throughout the workflow of the pipeline ensures the consistency, validity and accuracy of results. Our pipeline is streamlined to maximize sensitivity without sacrificing specificity. We have incorporated a number of reference population databases and mutation databases including, but not limited, to 1000 Genomes Project, gnomAD, ClinVar and HGMD into our clinical interpretation software to make the process effective and efficient. For missense variants, *in silico* variant prediction tools such as SIFT, PolyPhen,MutationTaster are used to assist with variant classification. Through our online ordering and statement reporting system, Nucleus, ordering providers have access to the details of the analysis, including patient specific sequencing metrics, a gene level coverage plot and a list of regions with suboptimal coverage (<20X for nuclear genes and <1000X for mtDNA) if applicable. This reflects our mission to build fully transparent diagnostics where ordering providers can easily visualize the crucial details of the analysis process.

Clinical Interpretation

We provide customers with the most comprehensive clinical report available on the market. Clinical interpretation requires a fundamental understanding of clinical genetics and genetic principles. At Blueprint Genetics, our PhD molecular geneticists, medical geneticists and clinical consultants prepare the clinical statement together by evaluating the identified variants in the context of the phenotypic information provided in the requisition form. Our goal is to provide clinically meaningful statements that are understandable for all medical professionals regardless of whether they have formal training in genetics.

Variant classification is the corner stone of clinical interpretation and resulting patient management decisions. Our classifications follow the ACMG guideline 2015.

The final step in the analysis is orthogonal confirmation. Sequence and copy number variants classified as pathogenic, likely pathogenic and variants of uncertain significance (VUS) are confirmed using bi-directional Sanger sequencing or by orthogonal methods such as qPCR/ddPCR when they do not meet our stringent NGS quality metrics for a true positive call.

Our clinical statement includes tables for sequencing and copy number variants that include basic variant information (genomic coordinates, HGVS nomenclature, zygosity, allele frequencies, in silico predictions, OMIM phenotypes and classification of the variant). In addition, the statement includes detailed descriptions of the variant, gene and phenotype(s) including the role of the specific gene in human disease, the mutation profile, information about the gene's variation in population cohorts and detailed information about related phenotypes. We also provide links to the references, abstracts and variant databases used to help ordering providers further evaluate the reported findings if desired. The conclusion summarizes all of the existing information and provides our rationale for the classification of the variant.

Identification of pathogenic or likely pathogenic variants in dominant disorders or their combinations in different alleles in recessive disorders are considered molecular confirmation of the clinical diagnosis. In these cases, family member testing can be used for risk stratification. We do not recommend using variants of uncertain significance (VUS) for family member risk stratification or patient management. Genetic counseling is recommended.

Our interpretation team analyzes millions of variants from thousands of individuals with rare diseases. Our internal database and our understanding of variants and related phenotypes increases with every case analyzed. Our laboratory is therefore well-positioned to re-classify previously reported variants as new information becomes available. If a variant previously reported by Blueprint Genetics is re-classified, our laboratory will issue a follow-up statement to the original ordering health care provider at no additional cost.

CPT code(s) *

81222, 81223, 81403, 81404 x3, 81405 x3, 81406 x4, 81407, 81479

* The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

ICD Codes

Refer to the most current version of ICD-10-CM manual for a complete list of ICD-10 codes.

Sample Requirements

- Blood (min. 1ml) in an EDTA tube
- Extracted DNA, min. 2 µg in TE buffer or equivalent
- Saliva (Please see Sample Requirements for accepted saliva kits)

Label the sample tube with your patient's name, date of birth and the date of sample collection.

We do not accept DNA samples isolated from formalin-fixed paraffin-embedded (FFPE) tissue. In addition, if the patient is affected with a hematological malignancy, DNA extracted from a non-hematological source (e.g. skin fibroblasts) is strongly recommended.

Please note that, in rare cases, mitochondrial genome (mtDNA) variants may not be detectable in blood or saliva in which case DNA extracted from post-mitotic tissue such as skeletal muscle may be a better option.

Read more about our sample requirements here.

For Patients

Other

- American Liver Foundation
- British Liver Trust
- British Liver Trust - Gilbert Sdr
- Canadian Liver Foundation
- Children's Liver Disease Foundation - Alagille Syndrome
- Children's Liver Disease Foundation - Progressive Familial Intrahepatic Cholestasis
- GeneReviews - ATP8B1 Deficiency
- GeneReviews - Alagille Syndrome
- GeneReviews - ATP8B1 Deficiency
- GeneReviews - Alagille syndrome
- ICP care
- Jesina D et al. Alagille Syndrome: An Overview. Neonatal Netw. 2017 Nov 1;36(6):343-347.
- NORD - Alagille Syndrome
- NORD - Crigler-Najjar syndrome
- NORD - Dubin-Johnson Syndrome
- NORD - Gilbert Syndrome
- NORD - Gilbert syndrome
- NORD - Progressive Familial Intrahepatic Cholestasis
- Nicastro E et al. Next generation sequencing in pediatric hepatology and liver transplantation. Liver Transpl. 2018 Feb;24(2):282-293.
- Progressive Familial Intrahepatic Cholestasis Web Group

- Reichert MC et al. Genetic determinants of cholangiopathies: Molecular and systems genetics. Biochim Biophys Acta. 2017 Jul 27. S0925-4439(17)30261-2.
- Stephens MC et al. Individualized Medicine in Gastroenterology and Hepatology. Mayo Clin Proc. 2017 May;92(5):810-825.
- The Alagille Syndrome Alliance
- Vitale G et al. Cryptogenic cholestasis in young and adults: ATP8B1, ABCB11, ABCB4, and TJP2 gene variants analysis by high-throughput sequencing. J Gastroenterol. 2017 Dec 13.
- van der Woerd WL et al. Current and future therapies for inherited cholestatic liver diseases. World J Gastroenterol. 2017 Feb 7;23(5):763-775.