Polycystic Liver Disease: **PRKCSH** Gene Deletion/Duplication

**Condition Description**

Polycystic liver disease (PCLD) is a dominantly inherited condition characterized by the presence of multiple liver cysts of biliary epithelial origin. Although the clinical presentation and histologic features of polycystic liver disease in the presence or absence of autosomal dominant polycystic kidney disease are indistinguishable, a genetically distinct form of isolated polycystic liver disease is known. Evidence supporting this idea includes a study in which 22 cases of either polycystic liver disease (PCLD) or polycystic kidney disease (PKD) that were found in 33,700 medicolegal autopsies were examined. Both organs were affected in only a single case. Cerebral hemorrhage was found only with adult PKD and was not observed in cases of only PCLD.

A study done on a single family traced the disorder through three generations, excluded the presence of kidney cysts, and excluded linkage of the disease in this family to the genetic markers of PKD1 and PKD2. The proband was a 61-year-old man with highly symptomatic PCLD, diagnosed at age 50. The patient's mother also had massive PCLD without known kidney disease; she died of cancer of unknown origin at age 80. The proband's sister had extensive PCLD with mild hepatomegaly and without kidney cysts. The proband's daughter had marked PCLD with normal liver size. The proband's son had no liver cysts. Information added in proof seemed to establish the autosomal dominant inheritance of the disorder: a 56-year-old maternal first cousin of the proband was found to have extensive PCLD with mild hepatomegaly without cysts in the kidneys, pancreas, or spleen. He presumably inherited the disorder from his father, the maternal uncle of the proband.

Autosomal dominant polycystic liver disease can be caused by mutation in the **PRKCSH** (19p13.2-p13.1) or the **SEC63** (6q21) gene. Mutations in **PRKCSH** and **SEC63** together account for less than one-third of autosomal dominant polycystic liver disease cases, indicating that there is at least one more locus associated with this disease.

For patients with suspected polycystic liver disease, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

Click here for the OMIM summary on this condition.

**Genes**

**PRKCSH**

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of polycystic liver disease in individuals who have tested negative for sequence analysis
- Individuals at-risk for polycystic liver disease due to family history who have tested negative for sequence analysis

**Methodology**

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region. Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Specimen Requirements**

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

### Special Instructions

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

### Related Tests

- Sequencing analysis of the *PRKCSH* gene is available and is required before deletion/duplication analysis.
- Custom diagnostic mutation analysis is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.