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 \textit{PRKCSH} (19p13.2-p13.1) or the \textit{SEC63} (6q21) gene. Mutations in \textit{PRKCSH} and \textit{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

\textbf{SEC63}

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of polycystic liver disease
- Individuals at-risk for polycystic liver disease due to family history

Methodology

PCR amplification of 5 exons contained in the \textit{SEC63} gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

Detection

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: ~99%

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

- Deletion/duplication analysis of the SEC63 gene by CGH array is available for those individuals in whom sequence analysis is negative.
- **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.