JAG1 Sequence Analysis for Alagille Syndrome

Alagille syndrome is a complex disorder characterized by cholestasis and bile duct paucity, cardiac defects, skeletal abnormalities, ophthalmologic abnormalities and characteristic facial features. Less common features of Alagille syndrome include kidney abnormalities, neurovascular accidents and pancreatic insufficiency. Developmental delay and mild mental retardation are seen in a minority of individuals with Alagille syndrome. Mutations in *JAG1* result in broad phenotypic variability, even within families.

Indications:

- Diagnostic testing in patients with suspected Alagille syndrome
- Targeted mutation analysis of at-risk relatives of patient with *JAG1* mutation
- Prenatal diagnosis of an at-risk fetus

Specimen:

At least 3 mls whole blood in purple top (EDTA) tube. Label tube with patient's name, birth date, and date of collection. Phlebotomist must initial tube to verify patient's identity.

Methodology:

TruSeq Custom Amplicon enrichment followed by next-generation sequencing with > 20 fold coverage at every target base and Sanger confirmation of all variants OR PCR-based sequencing, of all exons and exon/intron boundaries of the gene.

Clinical Sensitivity:

Sequencing of the coding regions and their exon/intron boundaries of the *JAG1* gene detects ~ 88% patients with Alagille syndrome. 20p12 microdeletion syndrome, which includes deletion of the entire *JAG1* gene, is identified in approximately 7% of patients with Alagille syndrome and can be detected by fluorescence in-situ hybridization (FISH) analysis. Mutations in *NOTCH2* are associated with Alagille syndrome in approximately 1% of affected individuals.

Analytical Sensitivity:

The sensitivity of DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed. Mutations in regulatory regions or other untranslated regions are not detected by this test. Multiple exon deletions, large insertions, genetic recombinational events and rare, primer site mutations may not be identified using this methodology. If the patient has received a liver transplant or recent blood transfusion, donor DNA may be present in the blood along with patient DNA (chimerism). In this case, additional testing may be required to rule out chimerism.

Turn-Around Times:

- 28 days

Costs:

Please call 1-866-450-4198 for pricing or with any billing questions.

Cincinnati Children's®

Human Genetics

Cytogenetic and Molecular Genetics Laboratory
CLIA#: 36D0656333
Phone: (513) 636-4474
Fax: (513) 636-4373
Email: moleculargenetics@cchmc.org
www.cincinnatichildrens.org/genetics

CPT Codes:

- ***JAG1* sequence analysis:** 81407
- **Family specific analysis:** 81403

Results:

Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for clinical management and additional testing, if warranted. Results will be reported to the referring physician or health care provider as specified on the test requisition form.

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 Friday.

Ship to:

Cytogenetics and Molecular Genetics Laboratories
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229
513-636-4474