## Lab Dept: Anatomic Pathology

## Test Name: ALAGILLE WATSON SYNDROME (JAG1) SEQUENCING

### *General Information*

**Lab Order Codes:** JAG1

**Synonyms:** Alagille Watson Syndrome; Cholestasis with Peripheral Pulmonary Stenosis; Arteriohepatic Dysplasia; Syndromatic Hepatic Ductular Hypoplasia; ALGS1

**CPT Codes:** Sequencing:
81407 – Molecular pathology Level 8
Deletion/Duplication- High Density Targeted Array
81406 – Molecular pathology Level 7

**Test Includes:** Analysis of bi-directional sequencing. Also includes a targeted array CGH analysis with exon-level resolution to evaluate for a deletion or duplication of one exon of this gene.

### *Logistics*

**Test Indications:** Alagille Syndrome is one of the major forms of chronic liver disease in children and is an autosomal dominant disorder with high penetrance but variable expressivity. The main clinical findings include cholestatis due to bile duct paucity, a characteristic facial appearance, and cardiovascular, eye and skeletal abnormalities. Cardiovascular findings include tetralogy of Fallot or singular manifestations thereof, peripheral pulmonary artery stenosis, atrial and/or ventricular septal defects, and coarction of the aorta. Butterfly vertebra is the most common skeletal finding. Other findings include narrowing of interpeduncular spaces in the lumbar spine, spina bifida occulta, and short fingers and ulnae. Facial features consist of broad forehead, triangular face, prominent zygomatic arch and moderate hypertelorism. Posterior embryotoxon and retinal pigmentary changes are common opthalmological findings. ALGS1 is caused by mutations in the JAG1 gene. It encodes jagged-1, a ligand for the Notch receptors. Notch proteins are transmembrane receptors and are components of signaling pathways important for cell fate. JAG1 is expressed in the developing heart and other structures affected in Alagille syndrome. Over 90% of patients with Alagille syndrome have a mutation in the JAG1 gene. Described JAG1 mutations include frameshift, missense, nonsense, splicing mutations and large deletions. DNA sequencing and coy number variation analysis are expected to identify about 90% and 5-7% of the JAG1 mutations, respectively.

**Lab Testing Sections:** Anatomic Pathology - Sendouts

**Referred to:** CTGT (MIM: 118450)

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| **Phone Numbers:** | MIN Lab: 612-813-6280<br><br>STP Lab: 651-220-6550 |
| **Test Availability:** | Daily, 24 hours (Preferred draws are Sunday - Thursday as specimens can only be received at the reference lab Monday - Friday. Specimens collected Friday or Saturday will be held refrigerated for shipment on Monday.) |
| **Turnaround Time:** | 3 to 6 weeks |
| **Special Instructions:** | A CTGT signed request form must be sent with any patient or specimen to the laboratory. |

## *Specimen*

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| **Specimen Type:** | Whole blood |
| **Container:** | Lavender top (EDTA) tube |
| **Draw Volume:** | 3 - 5 mL blood |
| **Processed Volume:** | Same as Draw Volume |
| **Collection:** | Routine venipuncture for blood specimens |
| **Special Processing:** | Lab Staff: Send whole blood in original collection container, including signed consent form and requisition, with a cool pack during warm temperatures, via overnight or second-day courier so that the sample will arrive at CTGT on a weekday (Monday through Friday). Samples drawn on Friday or Saturday should be held at refrigerated temperatures for shipment on Sunday or Monday. Specimens can be held at refrigerated temperatures for up to 7 days. **Do not** freeze. |
| **Patient Preparation:** | None |
| **Sample Rejection:** | Unrefrigerated specimens older than 48 hours for blood; frozen specimens; mislabeled or unlabeled specimens |

## *Interpretive*

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| **Reference Range:** | No mutations detected |
| **Critical Values:** | N/A |
| **Limitations:** | N/A |

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| **Methodology:** | Direct DNA sequencing of PCR products generated from genomic DNA. In all instances, sequencing of exons and exon-intron boundaries is performed for all genes. This is the gold standard for mutation detection in genes and is highly sensitive for point mutations, splice site mutations, and small exonic deletions, insertions and indels.<br><br>Deletion/Duplication by CTGT High-Density Targeted (HDT) Array |
| **References:** | CTGT November 2012<br>(484) 244-2900 Fax (484) 244-2904 |
| **Updates:** | 11/5/2012: Testing moved from GeneDx to CTGT. |