LifeLabs Genetics™

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Lab Director

Dr. Jane Doe
Hospital Name
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Final Report

Patient name:	PATIENT, SAMPLE	**Order no.:**	650000823
Patient no.:	10000054	**Reference no.:**	IV739292
DOB:	yyyy/mm/dd	**Specimen collected:**	yyyy/mm/dd
Sex:	Male	**Date approved:**	yyyy/mm/dd
Sample type:	Blood, EDTA	**Date reported:**	yyyy/mm/dd

TEST REQUEST: JAG1 (OMIM: 601920) sequencing analysis; Alagille syndrome (OMIM: 118450); inheritance: autosomal dominant.

CLINICAL INFORMATION: Infant male presenting with cholestasis and renal dysplasia. Ophthalmology pending.

A diagnosis of Alagille syndrome cannot be genetically confirmed.

TEST RESULT:

Gene (OMIM)	Inheritance	Variant	Classification
JAG1 (601920)	Autosomal dominant	No pathogenic variant	--

INTERPRETATION:

We did not detect any pathogenic variants in the JAG1 gene by sequencing. However, large deletions/duplications not detectable by sequencing have been reported in the JAG1 gene. Therefore, **we recommend proceeding to MLPA analysis of JAG1 to test for these additional mutations.** Please note that Alagille syndrome is inherited in an autosomal dominant manner, and that the JAG1 gene is reported to account for 94-96% of Alagille syndrome cases (NCBI GeneReviews 2013; PMID: 20301450).

Our genetic counsellors are available to assist you with interpretation of these results. Alternately, to locate genetic services near you, please visit the Canadian Association of Genetic Counsellors website at www.cagc-accg.ca.

RECOMMENDATIONS:
-Consider proceeding to large deletion/duplication (MLPA) analysis of the JAG1 gene.
-Genetic counselling.

Please note that any further analyses will result in additional costs.

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ADDITIONAL INFORMATION:
This test has been developed and validated for clinical purposes by Centogene AG and LifeLabs Genetics. Variants are classified on the basis of multiple private and public databases – including CentoMD™, NCBI 1000 genomes, NHLBI Exome Sequencing Project, Exome Aggregation Consortium and HGMD® Professional – and in accordance with ACMG 2015 guidelines (PMID: 25741868).

Scientific use of these results requires permission from Centogene and LifeLabs Genetics. More information is available at www.lifelabsgenetics.com or Ask.Genetics@LifeLabs.com.

Categories of variant classification (ACMG categories):
Class 1 - Pathogenic variant (sufficient evidence for pathogenicity)
Class 2 - Likely pathogenic variant (strong evidence for pathogenicity)
Class 3 - Variant of uncertain clinical significance (insufficient or conflicting evidence regarding variant effect)
Class 4 - Likely benign variant (strong evidence for neutrality)
Class 5 - Benign variant (sufficient evidence for neutrality)

METHODS:
The **JAG1** gene was analysed by PCR and sequencing of both DNA strands of the entire coding region and the highly conserved exon-intron splice junctions. The reference sequence of the **JAG1** gene is: **NM_000214.2**. **Please note that large deletions, duplications, and novel deep intronic variants may not be detectable by the techniques applied.**

All **Class 1 and 2** pathogenic variants are confirmed by forward and reverse Sanger sequencing of an independent aliquot of DNA.

Please note:

- Analysis and interpretation are based upon the assumption that the patient's medical and family history is accurate as described.
- Common polymorphisms have not been included in this report. A complete list of any detected Class 4 and 5 variants is available upon request.
- All technical protocols have limitations that affect specificity. Polymorphic/normal genomic variation in the patient sample may interfere with mutation detection, and lab error is a rare but possible occurrence. Please contact us if these results appear inconsistent with the clinical evidence.
- Results and interpretation are based upon current technologies, methodologies and medical literature, which may change over time with progress in the field. Please stay in contact with us to remain up to date on options for follow-up testing.

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LifeLabs Genetics is licensed by the Ontario Ministry of Health and Long-Term Care to operate as a clinical genetic laboratory: MOHLTC license 5806. If you have any questions or would like to inquire about additional analyses, please do not hesitate to contact us at **Ask.Genetics@lifelabs.com** or call us at **1-84-GENE-HELP** (1-844-363-4357).