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Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	[redacted]
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Cystic Fibrosis (CFTR) Sequencing with Reflex to Deletion/Duplication

ARUP test code 0051640

Cystic Fibrosis Seq, w/Rflx DelDup Spec	Whole Blood
Cystic Fibrosis Seq, w/Rflx DelDup Int	See Note *

TEST PERFORMED - 0051640
TEST DESCRIPTION - Cystic Fibrosis (CFTR) Sequencing with Reflex to Deletion/Duplication
INDICATION FOR TEST - Confirm Diagnosis

RESULT
One pathogenic variant was detected in the CFTR gene.

DNA VARIANT
Classification: Pathogenic
Gene: CFTR
Nucleic Acid Change: c.2601dupA; Heterozygous
Amino Acid Alteration: p.Val868fs

INTERPRETATION
According to information provided to ARUP, this individual has had a borderline sweat chloride test as well as a family history of cystic fibrosis. One copy of the pathogenic variant, c.2601dupA; p.Val868fs, was detected in the CFTR gene by sequencing. No pathogenic CFTR variants were detected by deletion/duplication analysis. This individual appears to be only a carrier of cystic fibrosis (CF); although the small possibility of an undetected CFTR variant (e.g., deep intronic or regulatory region) has not been excluded. If an additional pathogenic variant, not detected by the current assay, is present on the opposite chromosome, this individual may be affected with CF.

Evidence for variant classification: The CFTR c.2601dupA; p.Val868fs variant (rs397508405), also known as c.2732insA, is reported in the literature in individuals affected with cystic fibrosis who carry a second pathogenic CFTR variant (see links to CFTR2 and cystic fibrosis mutation databases; McGinniss 2005). This variant is reported in ClinVar (Variation ID: 487396), and is absent from general population databases (Exome Variant Server, Genome Aggregation Database), indicating it is not a common polymorphism. This variant causes a frameshift by inserting a single nucleotide, so it is predicted to result in a truncated protein or mRNA subject to nonsense-mediated decay. Additionally, several downstream truncating variants have been described in individuals with cystic fibrosis and are considered pathogenic (McGinniss 2005, Sosnay 2013). Based on available information, this variant is considered to be pathogenic.

RECOMMENDATIONS

H=High, L=Low, *=Abnormal, C=Critical

Medical management should rely on clinical findings and family history. Genetic consultation is indicated. For optimal interpretation, this result must be correlated with all the results from this family to confirm that the variant causing disease in this family is detectable by this assay. Offer adult family members carrier testing for the identified CFTR variant (Familial Mutation, Targeted Sequencing, ARUP test code 2001961).

COMMENTS
Reference Sequence: GenBank # NM_000492.3 (CFTR)
Nucleotide numbering begins at the "A" of the ATG initiation codon.
Likely benign and benign variants are not included in this report.

REFERENCES
Link to CFTR2 database: https://cftr2.org/
Link to cystic fibrosis mutation database for c.2601dupA: http://www.genet.sickkids.on.ca/cftr/MutationDetailPage.external?sp=1081
McGinniss MJ et al. Extensive sequencing of the CFTR gene: lessons learned from the first 157 patient samples. Hum Genet. 2005 Dec;118(3-4):331-8.
Sosnay PR et al. Defining the disease liability of variants in the cystic fibrosis transmembrane conductance regulator gene. Nat Genet. 2013 Oct;45(10):1160-7.

This result has been reviewed and approved by Weimin Sun, Ph.D.

H=High, L=Low, *=Abnormal, C=Critical

BACKGROUND INFORMATION: Cystic Fibrosis (CFTR) Sequencing with Reflex to Deletion/Duplication
CHARACTERISTICS: Chronic sino-pulmonary disease, gastrointestinal malabsorption/pancreatic insufficiency, and obstructive azoospermia. Findings are often limited to a single organ system such as isolated pancreatitis, bilateral absence of the vas deferens, nasal polyposis, or bronchiectasis in non-classic cystic fibrosis (CF).
INCIDENCE OF CLASSIC CF: 1 in 3,000 Caucasians or Ashkenazi Jewish, 1 in 8,000 Hispanics, 1 in 15,000 African Americans, 1 in 32,000 Asians.
INCIDENCE OF NONCLASSIC CF: Unknown.
INHERITANCE: Autosomal recessive.
PENETRANCE: High for severe mutations, variable for mild/moderate mutations.
CAUSE OF CLASSIC CF: Two deleterious CFTR mutations on opposite chromosomes.
CAUSE OF NONCLASSIC CF: Typically one severe and one mild/moderate CFTR mutations on opposite chromosomes.
MUTATIONS TESTED: Base pair substitutions and deletions/duplications within the coding region and intron-exon boundaries; additionally, two deep intronic mutations (3849+10kbC>T and 1811+1.6kbA>G).
CLINICAL SENSITIVITY: 99 percent.
METHODOLOGY FOR SEQUENCING: Bidirectional sequencing of the entire CFTR coding region, intron-exon boundaries and two deep intronic mutations.
METHODOLOGY FOR DELETION/DUPLICATION: Multiplex ligation-dependent probe amplification (MLPA) to detect large CFTR coding region deletions/duplications.
ANALYTICAL SENSITIVITY AND SPECIFICITY FOR SEQUENCING: 99 percent.
ANALYTICAL SENSITIVITY AND SPECIFICITY FOR MLPA: 98 percent.
LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. Breakpoints for large deletions/duplications will not be determined. Regulatory region and some deep intronic mutations will not be detected.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online at www.aruplab.com.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Cystic Fibrosis Seq, w/Rflx DelDup Spec	19-254-401771	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Cystic Fibrosis Seq, w/Rflx DelDup Int	19-254-401771	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical