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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	6/30/2000
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	

PTEN-Related Disorders (PTEN) Sequencing

ARUP test code 2002722

PTEN FGS Specimen	Whole Blood	
PTEN-Related Disorders Interpretation	**Positive**	*

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

TEST PERFORMED - 2002722
TEST DESCRIPTION - PTEN-Related Disorders (PTEN) Sequencing
INDICATION FOR TEST - Confirm Diagnosis

RESULT
One pathogenic variant was detected in the PTEN gene.

DNA VARIANT
Classification: Pathogenic
Gene: PTEN
Nucleic Acid Change: c.733C>T; Heterozygous
Amino Acid Alteration: p.Gln245Ter

INTERPRETATION
One pathogenic variant, c.733C>T; p.Gln245Ter, was detected in the PTEN gene by sequencing. This result is consistent with a diagnosis of PTEN hamartoma tumor syndrome (PHTS); clinical manifestations are highly variable and may be age-dependent.

Evidence for variant classification: The PTEN c.733C>T, p.Gln245Ter variant (rs786202918) has been reported in multiple individuals with Cowden disease or Bannayan-Riley-Ruvalcaba syndrome (Hansen-Kiss 2017, Marsh 1998, Sarquis 2006). It is listed as pathogenic in ClinVar (Variation ID: 186396), and observed once in the Genome Aggregation Database general population database (1/246214 alleles). The variant introduces a premature termination codon, and is predicted to result in a truncated protein or an absent transcript. Based on the above information, the variant is classified as pathogenic.

RECOMMENDATION
Genetic consultation is recommended, including a discussion of medical screening and management. At-risk family members should be offered targeted sequencing for the identified PTEN variant (Familial Mutation, Targeted Sequencing; ARUP test code 2001961).

COMMENTS
Reference Sequence: GenBank # NM_000314.4 (PTEN)
Nucleotide numbering begins at the "A" of the ATG initiation codon.
Benign variants are not included in this report but are available upon request.

REFERENCES
Link to variant in ClinVar:
https://www.ncbi.nlm.nih.gov/clinvar/variation/186396/

Hansen-Kiss E et al. A retrospective chart review of the features of PTEN hamartoma tumour syndrome in children. J Med Genet. 2017 pii: jmedgenet-2016-104484

Marsh D et al. Mutation spectrum and genotype-phenotype analyses in Cowden disease and Bannayan-Zonana syndrome, two hamartoma syndromes with germline PTEN mutation. Hum Mol Genet. 1998; 7(3):507-15.

Sarquis M et al. Distinct expression profiles for PTEN transcript and its splice variants in Cowden syndrome and Bannayan-Riley-Ruvalcaba syndrome. Am J Hum Genet. 2006; 79(1):23-30.

This result has been reviewed and approved by Elaine Lyon, Ph.D.

BACKGROUND INFORMATION: PTEN-Related Disorders (PTEN) Sequencing

CHARACTERISTICS OF PTEN HAMARTOMA TUMOR SYNDROME (PHTS):
Clinical findings are highly variable and include Cowden syndrome (CS), Bannayan-Riley-Ruvalcaba syndrome(BRRS), Proteus syndrome (PS) and Proteus-like syndrome (PSL).
CS: Multiple hamartoma syndrome with increased risk for malignant and benign tumors of the breast, thyroid and endometrium. Other associated findings include macrocephaly and mucocutaneous lesions (facial trichilemmomas, palmoplantar keratoses and papillomatous papules).
BRRS: Characterized by macrocephaly, intestinal hamartomatous polyposis, lipomas, hemangiomas and pigmented macules of the glans penis.
PS: A progressive disorder demonstrating mosaic distribution of associated lesions. Findings include hamartomatous tissue overgrowth, hyperostoses, connective tissue and epidermal nevi, dysregulated adipose tissue, vascular malformations and other congenital malformations.
PSL: Describes individuals with significant features of PS who do not meet clinical diagnostic criteria for PS.
INCIDENCE: At least 1 in 200,000 for CS; PS is rare with approximately 120 reported cases; unknown for other PTEN-associated conditions.
INHERITANCE: Autosomal dominant. All mutations causing PS and 50-90 percent causing CS are de novo.
CAUSE: Pathogenic PTEN gene mutations.
PENETRANCE: 99 percent by 30 years of age for CS.
CLINICAL SENSITIVITY: 80 percent for CS, 60 percent for BRRS, 50 percent for PSL and 20 percent for PS.
METHODOLOGY: Bidirectional sequencing of the PTEN promoter, coding region and intron-exon boundaries.
ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.
LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. Some regulatory region mutations, deep intronic mutations, and large deletion/duplications will not be detected.

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

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
PTEN FGS Specimen	18-186-112572	7/5/2018 2:18:00 PM	7/5/2018 2:22:31 PM	7/5/2018 2:36:00 PM
PTEN-Related Disorders Interpretation	18-186-112572	7/5/2018 2:18:00 PM	7/5/2018 2:22:31 PM	7/5/2018 2:36:00 PM

END OF CHART

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