Test Patient
Sex Assigned at Birth: Female
Date of Birth: 01/01/1970
Sample ID: SM07668
Sample Type: BLOOD
Collection Date: 02/01/2024
Received Date: 02/03/2024

Clinic: Medical Genetics Center
Physician: Test Doctor, M.D.
Phone: 510-555-0000
NPI: 1234567890

Requisition ID:
RQ-0000059

Report Number:
RP220

Report Date:
09/30/2025

Scan to learn more

https://myome.com/r/?id=RP220

TEST INFORMATION

MyOme Rare Disease, Whole Genome Analysis, Proband

Indication for testing: Autism, Coloboma, Delayed speech and language development, Global developmental delay, Hirsutism, Hypoplasia of the corpus callosum, Macrocephaly, Partial agenesis of the corpus callosum, Postnatal growth retardation, joint hypermobility

Positive — Clinically relevant variant(s) detected

LOCATION	CONDITION (MODE OF INHERITANCE)	VARIANT	ZYGOSITY	INHERITED FROM	CLASSIFICATION
ARID1B	Coffin-Siris syndrome (Autosomal Dominant)	c.292A>G, p.(Tyr675Ter)	Heterozygous	Unknown	Likely Pathogenic

INTERPRETATION

A likely pathogenic variant was detected in the ARID1B gene.

A heterozygous likely pathogenic variant in the ARID1B gene was detected. Disease-causing variants in this gene are associated with Coffin-Siris syndrome which may be consistent with the individual's reported clinical features. Analysis of the patient's long-read sequencing data identified a methylation signature specific to Coffin-Siris syndrome. This finding indicates that the variant has a functional impact, thereby affirming a diagnosis consistent with the clinical presentation.

NEXT STEPS

- These results should be interpreted in the context of this individual's clinical findings, family history, and other laboratory data.
- Genetic counseling is recommended to discuss the significance of these results.

MyOme, Inc.
1505 Adams Drive, Suite B1
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

Report Information:
Test Patient
DOB: 01/01/1970
Requisition ID: RQ-0000059

Lab Director:
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502

VARIANT SUMMARY

ARID1B gene, NC_000006.12:g.156901413dup, NM_001374828.1:c.2024dup, p.(Tyr675Ter), Likely Pathogenic

EVIDENCE

The identified heterozygous duplication variant (p.Tyr675Ter) in the ARID1B gene results in a frameshift and consequent premature stop codon that is expected to trigger nonsense-mediated decay, leading to a truncated or absent protein. Loss-offunction variants are known to be pathogenic in ARID1B. This variant is absent from large population databases, including gnomAD. ClinVar does not have an entry for this variant. This variant has not been previously reported in the literature in individuals affected with ARID1B-related conditions. Based on the evidence above and according to the ACMG/AMP variant interpretation guidelines, this variant has been classified as Pathogenic.

Functional Analysis: This patient had long read sequencing for detection of the specific methylation signature associated with Coffin-Siris syndrome (eg ARID1B-related syndrome). The Coffin-Siris syndrome methylation signature was detected.

GENE INFORMATION

ARID1B encodes a component of the SWI/SNF chromatin remodeling complex which plays a role in cell-cycle activation, chromatin remodelling and transcriptional regulation. Pathogenic variants in ARID1B are known to cause autosomal dominant Coffin-Siris syndrome with clinical features that include impaired intellectual development associated with coarse facial features, hypertrichosis, sparse scalp hair, and hypoplastic or absent fifth fingernails or toenails. This condition typically has a highly variable phenotype and additional features may include poor overall growth, craniofacial abnormalities, spinal anomalies, and congenital heart defects (PMID: 25169447, 25169447).

MyOme, Inc.
1505 Adams Drive, Suite B1
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

Report Information:
Test Patient
DOB: 01/01/1970
Requisition ID: RQ-0000059

Lab Director:
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502

TEST METHODS

- Specimen receipt, accessioning, data analysis, and interpretation is performed by MyOme Inc., 1505 Adams Drive, Suite B1, Menlo Park, CA 94025, CLIA# 05D2203070. Whole Genome Sequencing, excluding data analysis and interpretation, is performed by Broad Clinical Labs LLC, 27 Blue Sky Dr, Burlington, MA 01803, CLIA#22D2055652.
- Genomic DNA obtained from submitted samples is sequenced using Illumina technology. Reads are aligned to the NCBI GRCh38 reference assembly.
- Information about the patient's phenotype is used to prioritize variants across a large number of genes. Variants are interpreted and reported based on the standards and guidelines set forth by the American College of Medical Genetics and Genomics (ACMG). Classification categories include pathogenic (P), likely pathogenic (LP), variants of unknown significance (VUS), likely benign (LB) and benign (B). Reported variants only include those which are classified as P, LP, or VUS, overlap with the tested individual's indication for testing and are consistent with the expected pattern of inheritance (when parental samples are submitted). For mitochondrial genome variants, only known P and LP variants are reported.
- Tandem repeat expansions (TREs) in the following genes are reported when they overlap the clinical indication for testing and fall within the reportable range: AFF2, AR, ATN1, ATXN1, ATXN2, ATXN3, ATXN7, ATXN8OS, C9orf72, CACNA1A, DIP2B, DMPK, FMR1, FXN, HTT, JPH3, LRP12, PABPN1, PPP2R2B, and TBP. This test does not report on the status of repeat expansion interruptions.
- All reported variants are confirmed, if necessary, by a secondary technology: SNVs are confirmed using Sanger sequencing; CNVs are confirmed using arrays, MLPA, PCR, or long-read sequencing, depending on the nature of the copy number variant; TREs are confirmed using long-read sequencing.
- Methylation analysis is performed using Oxford Nanopore long-read sequencing on genomic DNA from whole blood. Reads are aligned to the NCBI GRCh38 reference assembly, and methylation data is extracted via modified basecalling. Methylation analysis is performed as a reflex test when a VUS is identified in a gene for which a genome-wide methylation signature has been validated, or when a copy number variant or region of homozygosity associated with an imprinting condition, currently limited to Angelman syndrome and Prader-Willi syndrome, is identified. Methylation findings are incorporated as evidence towards the assessment and classification of variants identified by whole genome sequencing. The results of methylation analysis are used to provide functional epigenetic information to further support variant classification.
- For the mitochondrial genome, the following quality control metrics are generally achieved: an average read depth of >3,000x and a minimum acceptable read depth of 1000x. Heteroplasmy is estimated using variant allele fraction.
- Nuclear genome mean depth of coverage: 31.4X; 96.8% of bases with coverage of at least 10X.

MyOme, Inc.
1505 Adams Drive, Suite B1
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

Report Information:
Test Patient
DOB: 01/01/1970
Requisition ID: RQ-0000059

Lab Director:
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502

TEST LIMITATIONS

- This test is designed to detect clinically relevant single-nucleotide variants, small insertions and deletions, and copy number variants (CNVs) across the genome, single-nucleotide variants and small insertions and deletions in the mitochondrial genome, and tandem repeat expansion (TRE) in a select set of genes.
- There are certain regions that are not well covered and will not be analyzed such as segmentally duplicated regions.
- The sensitivity of this test to detect deletions and duplications may vary depending on the depth of coverage, the size of the variant or other inherent sequence properties. For example, sensitivity to detect all CNVs 50-100 bp in size and duplications < 1kb is reduced.
- This analysis does not detect balanced alterations (reciprocal translocations, Robertsonian translocations, inversions, and balanced insertions) or other complex structural variants, methylation abnormalities, genomic imbalances in segmentally duplicated regions, and mosaicism of the nuclear genome; possible cases of mosaicism may be investigated at the discretion of the laboratory director. Sensitivity to detect variants may be reduced in low complexity regions such as homopolymer regions.
- This analysis does not detect deletions, duplications, or complex rearrangements of the mitochondrial genome. Although sensitivity for detection of >5% heteroplasmic single-nucleotide variants is expected to be high based on validation studies, we cannot guarantee that these low-level heteroplasmic variants will always be identified due to paralogy with the nuclear genome.
- This analysis does not detect variants in the following regions in the mitochondrial genome: chrM:1-576, chrM:16024-16569.
- Methylation analysis is a reflex test and is only performed when a qualifying variant, copy number variant, or region of homozygosity is identified that meets the criteria described in the Methods section. Epimutations will not be detected.
- A history of stem cell or bone marrow transplantation, or recent blood transfusion may impact the accuracy of the results.
- Like most tests, this test carries a risk of false negative or false positive results, which may be caused by, without limitation, sample contamination from biological or non-biological sources, specimen marking issues, rare genetic variants interfering with analysis, and other technical issues and limitations.

DISCLAIMERS

- This test was developed, and its performance characteristics were determined, by MyOme, Inc., a clinical laboratory certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and College of American Pathologist (CAP) accredited to perform high complexity clinical laboratory testing. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA).
- Like most tests, this test carries a risk of false negative or false positive results. Testing is unavailable for samples damaged by human error, lost/destroyed due to weather, transit issues or other problems beyond the control of MyOme. Test results should always be interpreted by a clinician in the context of clinical and familial data with the availability of genetic counseling when appropriate. MyOme is not responsible for the content of third-party websites referenced in this report.
- The interpretation of variants is based on our current understanding of the genome. These interpretations may change over time as more information about these alterations becomes available. Possible diagnostic errors include variant call errors, sample misidentification, and other sources.

REVIEWED BY

MyOme Example Lab Director

09/30/2025

Date

MyOme, Inc.
1505 Adams Drive, Suite B1
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

Report Information:
Test Patient
DOB: 01/01/1970
Requisition ID: RQ-0000059

Lab Director:
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502