Rare Disease GENOME ANALYSIS

TEST CODE: PR51224, PR51235, PR51243

Overview

MyOme's whole-genome sequencing (WGS) evaluates protein coding and non-coding regions of the genome and includes copy number variant (CNV) analysis, mitochondrial genome analysis, and analysis of tandem repeat expansions (TREs) and methylation signatures for select variants. The whole-genome backbone enables the ability to re-query a patient's genome as new information becomes available.

Clinical Use

This test is for individuals with clinical features suggestive of a genetic cause, including neurodevelopmental disorders, multiple congenital anomalies, and epilepsy.

Method

- PCR-free library preparation with 2x150 base pair (bp) paired-end WGS of genomic DNA extracted from submitted samples to an average depth of 30X or greater
- Identification of single-nucleotide variants (SNVs), small insertions and deletions (indels), and CNVs in coding regions and non-coding regions across the nuclear genome
- Identification of SNVs and small insertions and deletions across the mitochondrial genome
- TRE and methylation signature analysis for select set of genes (see Tables 1 and 2 on back)
- Interpretation and reporting based on ACMG guidelines, patient clinical indication, and familial samples (when provided)

Sample Types

- Blood (2 EDTA tubes)
- Buccal (2 swabs)

Turnaround Times

- From sample received, most results are delivered in 5-6 weeks.*
- Follow-up testing or re-requisitions are typically completed within 2-3 weeks.

Included

- Confirmation of reported variants, as needed, by a secondary technology
- Secondary analysis of TREs using long-read sequencing
- Secondary analysis of methylation patterns to distinguish between imprinting conditions or aid in interpretation of variants of uncertain significance (VUS)
- Comprehensive report with pathogenic variants, likely pathogenic variants, and VUS correlated with the patient's phenotype
- Option for post-test genetic counseling

Test Performance**

Nuclear Genome

- >99.5% exonic regions covered by ≥10X
- >99% sensitivity for SNVs and indels
- 98% sensitivity for benchmark CNVs >1 kb in size

Mitochondrial Genome

- Mean coverage depth of 3000X or greater (minimum acceptable is 1000X)

*Turnaround times are provided as estimates and begin once sample(s) are processed at MyOme. Turnaround times may be extended in cases outside of MyOme's control, including delays related to confirmation testing or other unforseen circumstances. **MyOme, Inc. (Data on File)

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Table 1: TRE Reportable Ranges for Genes Analyzed

Key

= Potentially reportable based on patient phenotype

= No associated phenotype, not reportable

Gene	Condition	Pathogenic*	Premutation	Intermediate	Uncertain	Normal
AFF2	Non-syndromic X-linked intellectual disability	>200	61–200			≤60
AR	Spinal and bulbar muscular atrophy	≥35				≤34
ATN1	Dentatorubral-pallidoluysian atrophy	≥48		36–47		≤35
ATXN1	Spinocerebellar ataxia 1	≥39		36–38		≤35
ATXN2	Spinocerebellar ataxia 2	≥33			31–32	≤30
ATXN3	Spinocerebellar ataxia 3	≥60		45–59		≤44
ATXN7	Spinocerebellar ataxia 7	≥34	28–33		20–27	≤19
ATXN8OS	Spinocerebellar ataxia 8	≥80			51–79	≤50
C9orf72	Frontotemporal dementia and/or amyotrophic lateral sclerosis	≥60			25–60	≤24
CACNA1A	Spinocerebellar ataxia 6	≥20	19			≤18
DIP2B	FRA12A intellectual disability	≥351			24–350	≤23
DMPK	Myotonic dystrophy 1	≥50	35–49			≤34
FMR1	Fragile X Syndrome; Fragile X-associated tremor/ataxia syndrome	≥201	55–200			≤54
FXN	Friedreich ataxia	≥66	34–43		44–65	≤33
HTT	Huntington disease	≥36				≤35
JPH3	Huntington disease-like 2	≥40			29–39	≤28
LRP12	Oculopharyngodistal myopathy 1	≥60			46–59	≤45
PABPN1	Oculopharyngeal muscular dystrophy	≥11				≤10
PPP2R2B	Spinocerebellar ataxia 12	≥43			33–42	≤32
TBP	Spinocerebellar ataxia 17	≥41				≤40

*Includes ranges associated with reduced penetrance

Table 2: Conditions Included in Methylation Signature Analysis

Gene/Location	Condition	Description	Purpose of Methylation Analysis
15q11-q13	Prader-Willi Syndrome (PWS)	Imprinting Conditions	Distinguish between two conditions with shared genetic locus
	Angelman Syndrome (AS)		
NSD1	Sotos Syndrome	Methylation-related Conditions	Provide functional information to aid in interpretation of VUS
ARID1A, ARID1B, ARID2, SMARCA4	Coffin-Siris Syndrome (CSS)		

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). 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 or accuracy of third-party websites.