myome® | Rare Disease



Our Genome-First Approach in Action

At MyOme, our mission is to deliver advanced diagnostic answers to empower families affected by rare disease, while enhancing care to improve outcomes. Join us as we walk through three patient stories* and highlight how our platform delivers superior performance to uncover diagnostic answers that other labs miss, finally connecting families to the answers and support they need.

*The patient stories described in this document are based on real-world clinical findings identified by MyOme genetic testing. To protect patient confidentiality, all identifying details have been removed or altered. Any images included are stock photography and do not depict actual patients.

Table of Contents

Background

Rare Disease Landscape

While individual rare diseases are uncommon, more than 10,000 distinct conditions collectively affect nearly 1 in 10 people.[1] Many rare diseases are severe, chronic, or life-threatening, making an accurate diagnosis critical.[2,3] For providers, a genetic diagnosis informs prognosis, recurrence risk, and treatment decisions. For families, it can bring clarity about what to expect, insights into which symptoms to monitor, and access to a supportive community of others facing the same condition.

Barriers to Diagnosis

Obtaining a genetic diagnosis is often slow and fragmented. Traditional gene panels are limited in scope and frequently miss critical variants, especially when a patient's symptoms don't fit a standard profile. Even when more advanced exome testing is ordered, traditional methods can leave gaps in coverage, leading to inconclusive results. These technical limitations force families into "diagnostic odysseys"—navigating multiple tests and providers before finally finding answers.

MyOme's Unified Multiomic Approach

Powered by **whole-genome sequencing (WGS)** and multiomic insights, MyOme's Rare Disease tests offer a more complete diagnostic picture than conventional methods. This "genome-first" approach increases diagnostic yield and delivers faster results, helping families move forward with a clear care plan.

1 in 10

people are affected by rare disease[1]

MyOme's Rare Disease Product Portfolio

MyOme offers flexible test options to meet the diagnostic needs of each patient. All tests use a whole-genome backbone, bringing genome-level features to copy number analysis and exome testing that improve diagnostic yield and enable earlier genetic diagnoses.

Available as:
- Proband (individual)
- Duo: +1 family member sample (parent or sibling)
- Trio: +2 family member samples (parent or sibling)

	Copy Number Analysis (CNA)	Exome	Genome
Genome-wide CNVs	✓	✓	✓
Exonic SNVs and indels		✓	✓
Tandem Repeat expansions (TREs)[a]	*Optional Fragile X add-on*	✓	✓
Methylation insights[b]		✓	✓
Mitochondrial DNA (mtDNA) variants[c]		✓	✓
Regions of homozygosity[d]		✓	✓
Uniparental disomy[d]		✓	✓
Intronic SNVs and indels			✓

[a] TRE analysis of 20 genes

[b] For select conditions

[c] Does not include mitochondrial CNVs

[d] For orders with parent samples (Duo/Trio)

MyOme's Unified, Multiomic, Genome-First Approach

Uniform, Genome-Wide Coverage Expands Variant Detection

Standard rare disease tests—like chromosomal microarray (CMA) and exome sequencing—rely on targeted enrichment of DNA regions, which can leave critical blind spots due to uneven probe/primer distribution, GC-bias, and exon-confined detection. MyOme's PCR-free WGS approach bypasses these technical limitations and expands coverage beyond exon boundaries to improve variant detection (**Table 1**).

Integrated Multiomic Analyses Increase Diagnostic Yield

Standard diagnostic tests require separate, often costly analyses for detection of non-nuclear or complex variants, including **tandem repeat expansions (TREs)**. MyOme integrates **mitochondrial DNA (mtDNA)** sequencing and **long-read sequencing (LRS)** into the primary diagnostic workflow to reduce costs, improve detection, and accelerate time-to-diagnosis (**Table 1**).

Seamless Reanalysis Powers Cost-Effective Insights

Beyond diagnostic breadth, MyOme's approach enables seamless reanalysis of the whole-genome dataset as clinical profiles evolve, new genetic discoveries are made, and detection algorithms advance. It also enables a streamlined upgrade to genome analysis, regardless of initial test ordered (**Table 1**).

Table 1. The technology that powers rare disease diagnosis.

Technology	Included in	Description	Enables
PCR-Free WGS 	• CNA • Exome • Genome	30X whole-genome backbone for diagnostic variant analysis	• Uniform, unbiased coverage of entire genome • Genome-wide CNV detection • Wider range of variants detected by Exome and Genome tests • Seamless reanalysis and test upgrades
Built-in mtDNA Sequencing 	• Exome • Genome	≥3,000X mean mtDNA coverage depth for diagnostic variant analysis	• Detection of mtDNA variants overlooked by standard nuclear-only tests
Automated LRS 	• CNA • Exome • Genome	For CNA, optional analysis of *FMR1* TRE is available For Exome and Genome Analysis, LRS is triggered when a TRE or methylation condition is suspected from WGS analysis	• Resolution and confirmation of 20 TREs for Exome and Genome tests • Detection of methylation patterns to help interpret variants or provide functional evidence that can re-classify variants of uncertain significance (VUS)

Rare Disease Genome Outperforms Targeted Panels for Atypical Presentations

A teenage girl presented with a clinical diagnosis of spasticity and cerebral palsy, microcephaly, and significant central motor dysfunction. No peripheral muscle weakness was observed.

The Limitations of Targeted Testing

Based on these phenotypes, clinicians ordered a targeted neuromuscular gene panel, which returned negative results and left the family without a molecular diagnosis (**Fig. 1**).

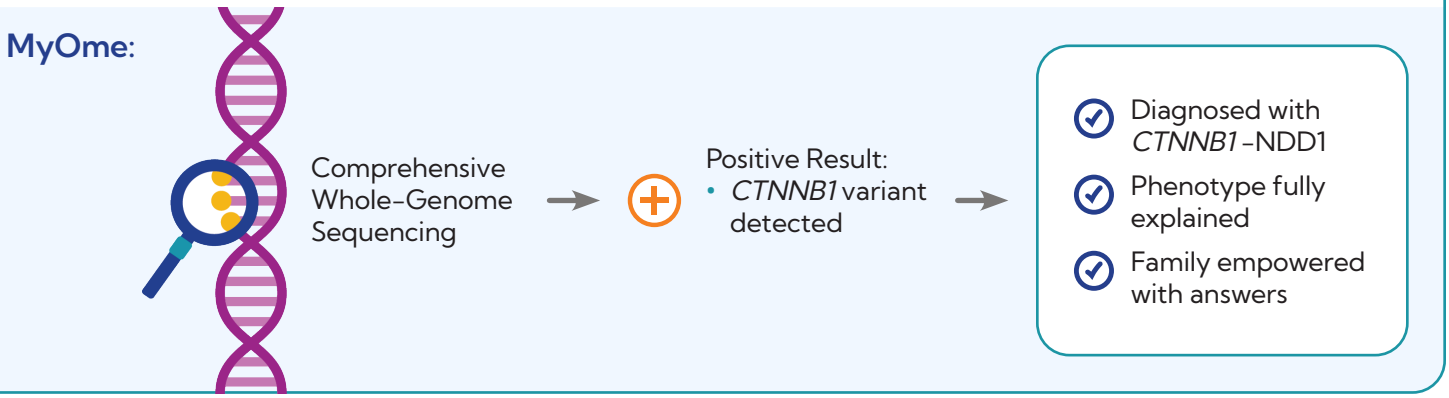
Narrow gene panels artificially restrict analysis to a single diagnostic category. In this case, the neuromuscular panel excluded genes associated with neurodevelopmental disorders, creating a "panel gap" that missed the underlying etiology.

Figure 1. Another lab's neuromuscular gene panel did not detect a relevant pathogenic variant.

The MyOme Solution

Following the negative panel test, Rare Disease Genome Analysis was performed. MyOme tests maximize diagnostic yield using phenotype-driven analysis with a genome-wide view, eliminating the "panel gap" to ensure relevant genes are not overlooked. MyOme's 30X PCR-free genome backbone identified a pathogenic *CTNNB1* variant, providing a definitive diagnosis of *CTNNB1*-related Neurodevelopmental Disorder 1 (NDD1) that fully explained the patient's phenotype. This result provided the long-sought diagnosis needed to initiate a more personalized plan of care (**Fig. 2**).

Figure 2. MyOme Genome Analysis detected a diagnostic variant associated with *CTNNB1*.

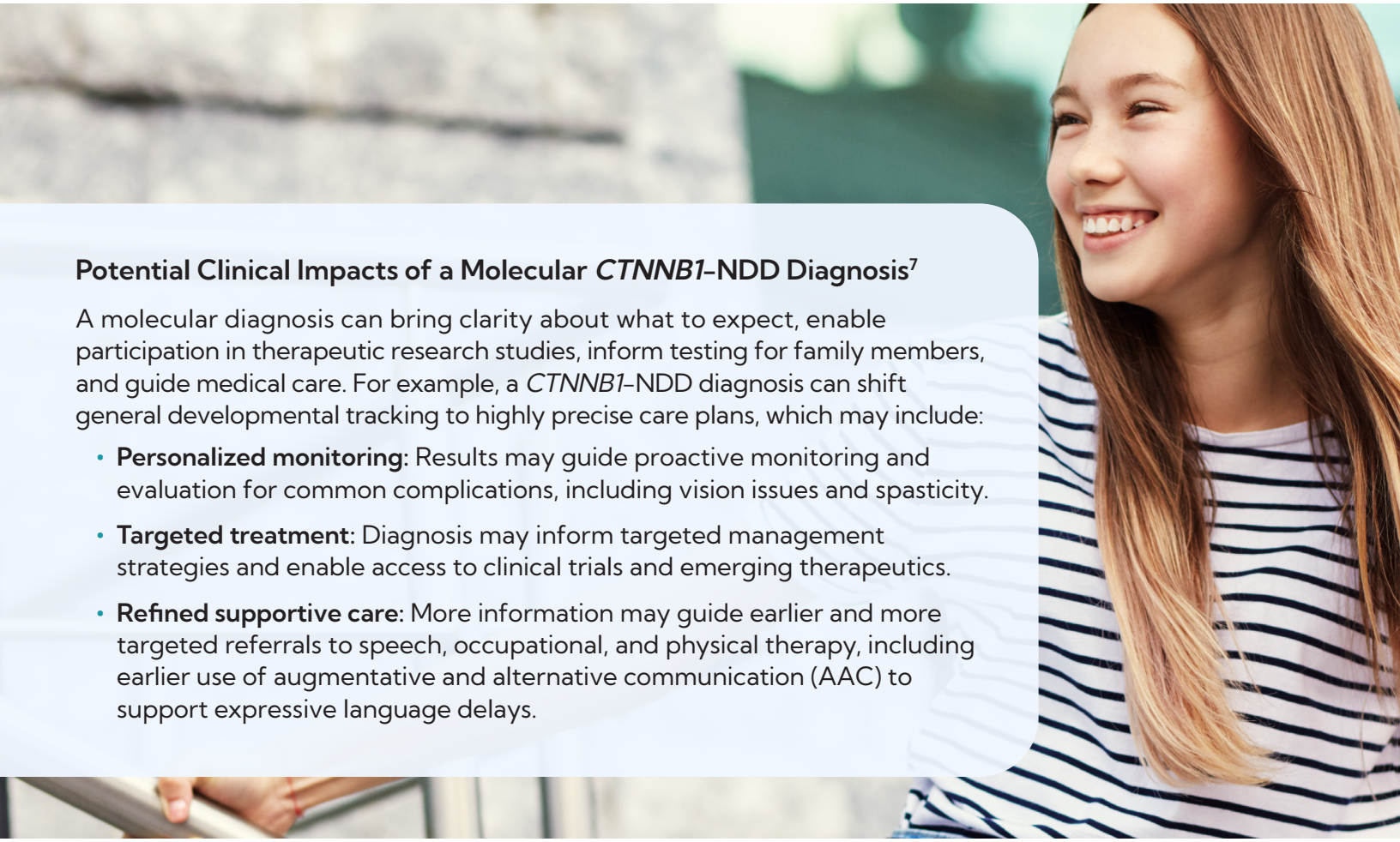


How MyOme Rare Disease Tests Outperform Traditional Gene Panels

MyOme's genome-first framework eliminates the need for guesswork with panel selection, providing a more comprehensive view of pathogenic variants across a broader range of conditions and increasing diagnostic yield (**Table 2**).

Table 2. Targeted Gene Panels vs. MyOme Genome Analysis.

	Traditional Gene Panels	MyOme Genome Analysis
Testing Scope	Narrow; limited to pre-defined genes	Comprehensive; analyzes entire genome
Diagnostic Breadth	Restricted to specific, suspected phenotypes	Unbiased; captures variants across overlapping conditions
Guideline Adherence[4-6]		
• **ACMG**	Second-Tier	Recommended First-Line
• **AAP**	De-prioritized	
• **NSGC**	Supportive for certain phenotypes	
Time-to-Diagnosis	Delayed by sequential steps	Accelerated by comprehensive approach



Potential Clinical Impacts of a Molecular *CTNNB1*-NDD Diagnosis[7]

A molecular diagnosis can bring clarity about what to expect, enable participation in therapeutic research studies, inform testing for family members, and guide medical care. For example, a *CTNNB1*-NDD diagnosis can shift general developmental tracking to highly precise care plans, which may include:

- **Personalized monitoring:** Results may guide proactive monitoring and evaluation for common complications, including vision issues and spasticity.
- **Targeted treatment:** Diagnosis may inform targeted management strategies and enable access to clinical trials and emerging therapeutics.
- **Refined supportive care:** More information may guide earlier and more targeted referrals to speech, occupational, and physical therapy, including earlier use of augmentative and alternative communication (AAC) to support expressive language delays.

MyOme's Genome-First Exome Detects More than Traditional Exome Tests

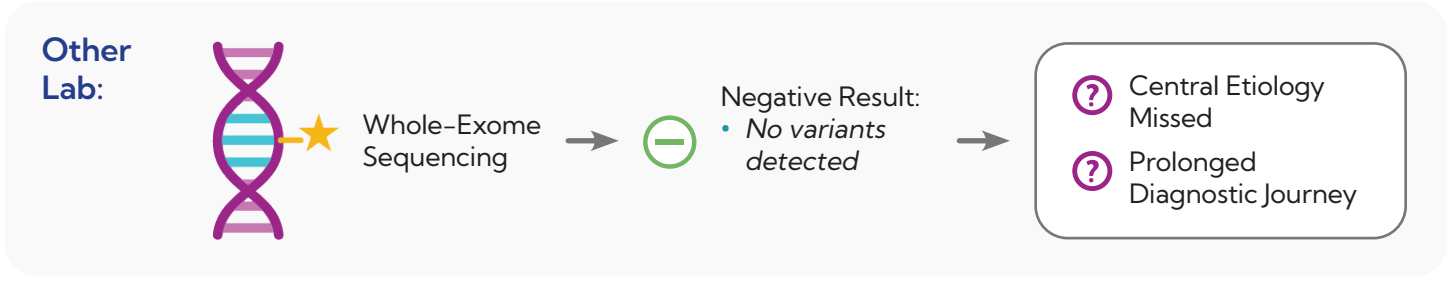
An 8-year-old boy presented with a complex phenotype: congenital hypotonia, autism spectrum disorder, global developmental delay, and gait abnormalities.

The Limitations of Standard Exome Capture

A traditional diagnostic exome conducted by another lab returned negative results, and left the family searching for answers (**Fig. 3**).

Standard methods, like whole-exome sequencing (WES) have key limitations: they only analyze predefined regions of the genome, struggle with complex areas like GC-rich sequences, and produce uneven coverage that makes it difficult to reliably detect certain variants, particularly small deletions (1-10kb range). Together, these technical constraints result in WES missing approximately 1% of pathogenic variants.[8]

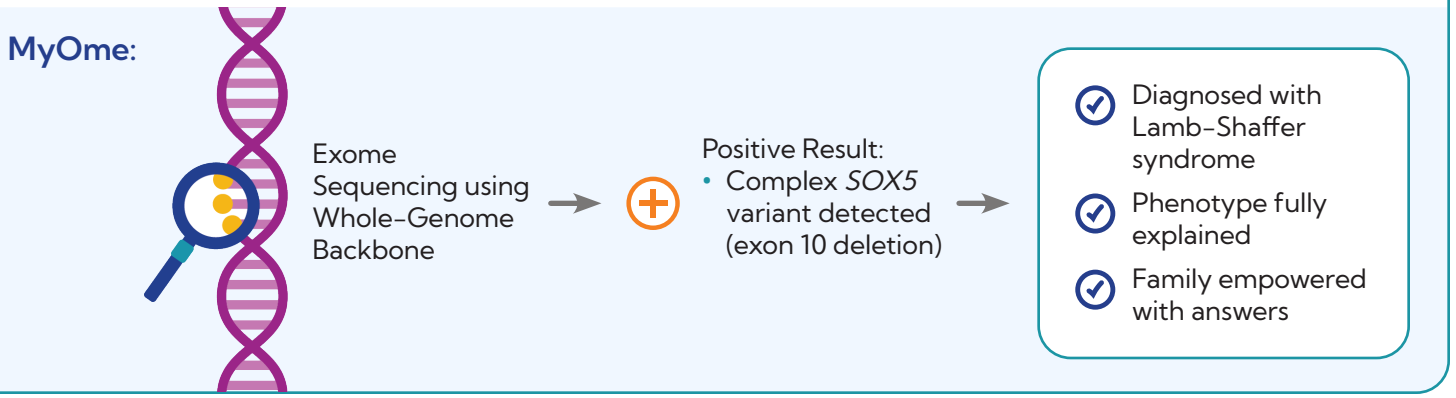
Figure 3. Another lab's exome tests did not detect a relevant diagnostic variant.



The MyOme Solution

Following the negative result of another lab's whole-exome analysis, MyOme Exome Analysis identified a diagnostic *SOX5* variant, associated with Lamb-Shaffer Syndrome. This finding finally ended an 8-year diagnostic odyssey, empowering the family with answers and enabling access to personalized clinical management (**Fig. 4**).

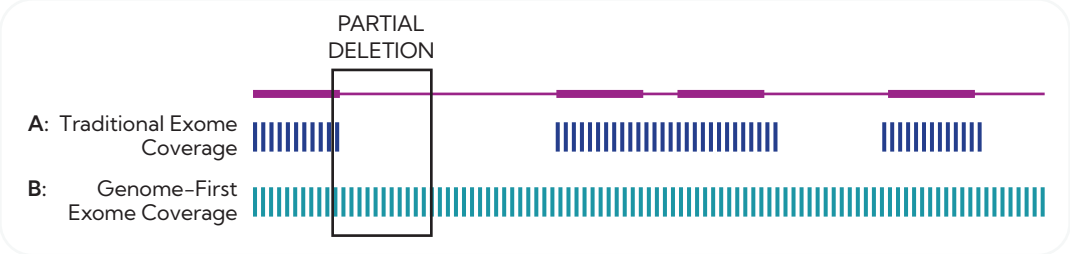
Figure 4. MyOme Exome Analysis detected a diagnostic deletion in the *SOX5* gene.



How MyOme Rare Disease Exome Analysis Outperforms Traditional Exome Tests

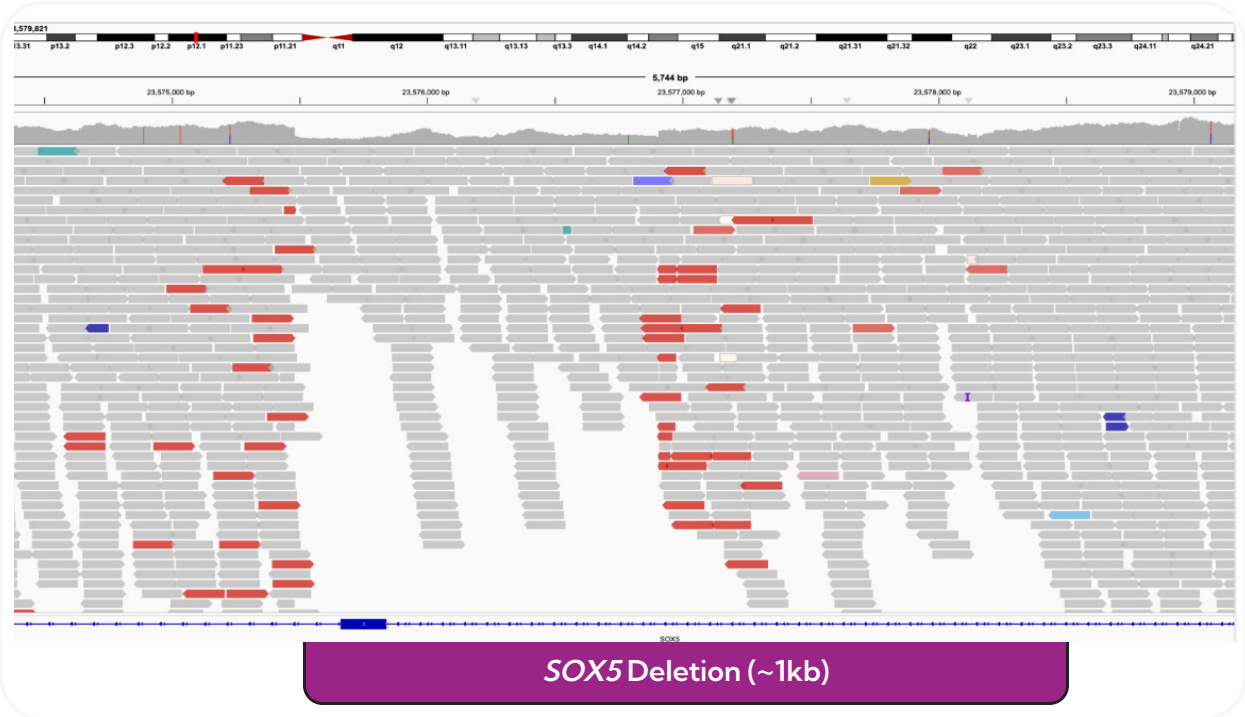
MyOme's Rare Disease Exome tests improve diagnostic yield by using a whole-genome backbone that provides more consistent coverage and fewer gaps compared to traditional hybrid-capture methods. This ensures deeper, more uniform coverage that extends beyond exon boundaries—removing "blind spots" and detecting variants that span intronic and intergenic boundaries (**Fig. 4**).

Figure 4. Traditional exome sequencing (A) covers only exonic regions, missing deletions that extend into intronic boundaries. MyOme's genome-first Exome (B) provides coverage across both exons and introns, enabling detection of these variants.



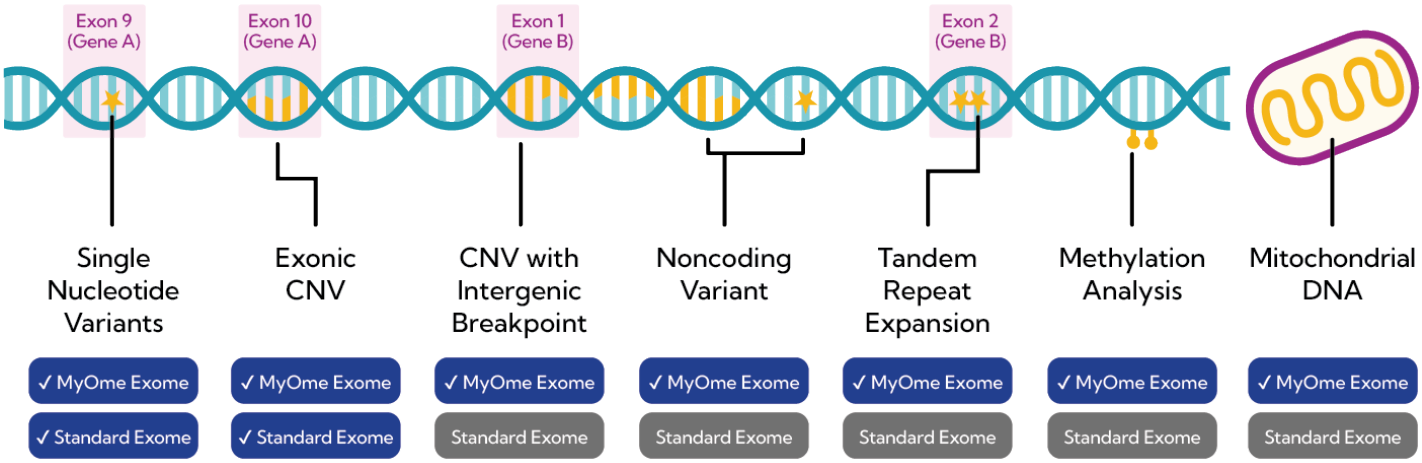
MyOme's Exome achieves superior breakpoint resolution by using paired-end reads combined with depth and split-read data. This identified the exact genomic coordinates where a sequence terminates and restarts, pinpointing small deletions that are often missed by traditional exome platforms. Using this methodology, MyOme's CNV caller successfully identified a ~1kb pathogenic deletion in *SOX5* with intronic breakpoints, which was missed by prior testing (**Fig. 5**).

Figure 5. Detection of a ~1kb intronic *SOX5* deletion by MyOme Exome Analysis — missed by prior exome testing.



In addition to improved coverage and superior breakpoint resolution, MyOme Exome Analysis integrates multiomic analyses, including mtDNA analysis (mean depth ≥3000x) and integrated long-read sequencing (LRS). LRS is conducted to confirm TREs and analyze methylation signatures in certain cases. Methylation results can be used to (1) re-classify VUS in genes associated with certain methylation-related conditions by providing the functional evidence needed to resolve the variant(s) and (2) confirm imprinting conditions that can be distinguished based on methylation profiles. Together, MyOme's genome-first coverage and multiomic analysis platform expands the breadth of variant types detected and improves variant resolution, enabling higher diagnostic yield compared to standard exomes (**Fig 6**).

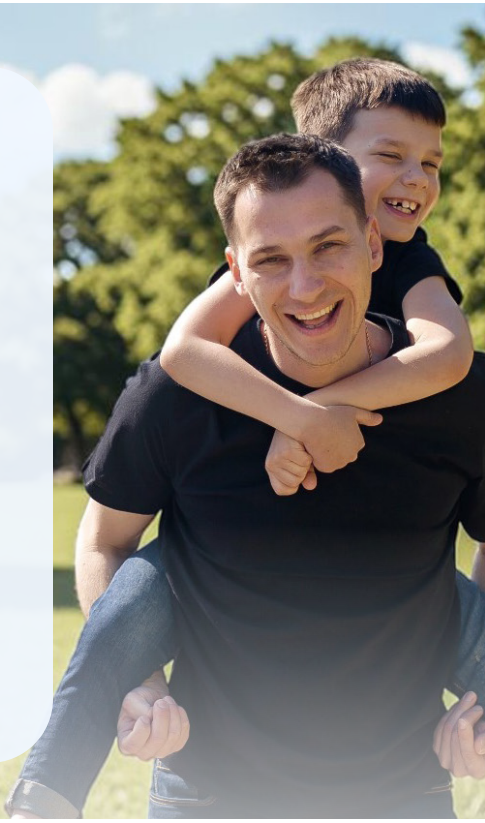
Figure 6. MyOme Rare Disease Exome Analysis detects more variant types than standard exome tests.



Potential Clinical Impact of a Molecular SOX5 (Lamb-Shaffer Syndrome) Diagnosis[9]

Providing a family with a molecular diagnosis brings long-awaited clarity and answers. In this case, a molecular diagnosis of Lamb-Shaffer Syndrome can enable:

- **Specialized monitoring:** Diagnosis may guide proactive monitoring and evaluation for common complications, including speech and language delays, behavioral and psychiatric features, and seizures.
- **Coordinated care:** More information may streamline multidisciplinary care and provide the family with syndrome-specific resources and support networks.
- **Reproductive insights:** Results may define recurrence risk for parents and informing testing strategies for biological siblings.



Integrated Long-Read Sequencing Improves Exome and Genome Performance

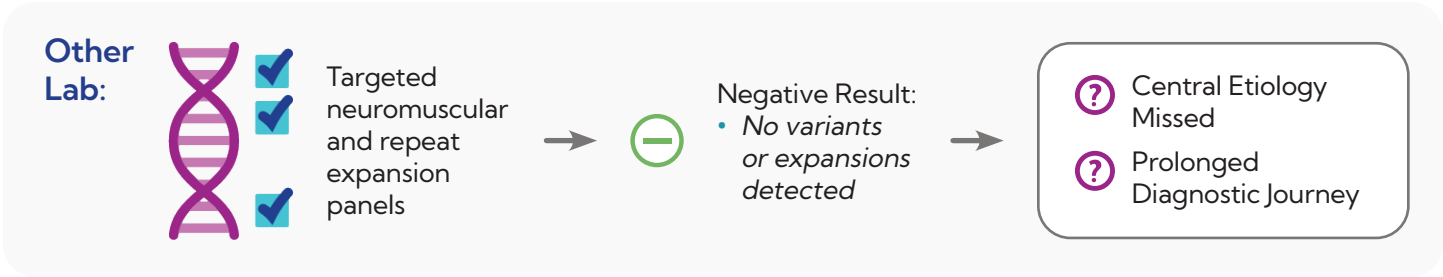
A 24-year old male presented with with muscle spasms and myotonia beginning at age 22, with a personal and family history of early-onset cataracts — a hallmark feature or myotonic dystrophies.

The Limitations of TRE Panels and Short-Read WGS

Prior testing by another lab included multiple neuromuscular and repeat expansion panels, including myotonic dystrophy analysis, but returned negative results (**Fig. 7**).

Traditional repeat panels use fragment analysis or repeat-primed PCR, which frequently fail to amplify large pathogenic expansions due to "allelic dropout," whereby the assay only detects the shorter, healthy allele—leading to false-negative results.

Figure 7. Another lab's targeted panels did not detect relevant pathogenic variants or expansions.



The MyOme Solution

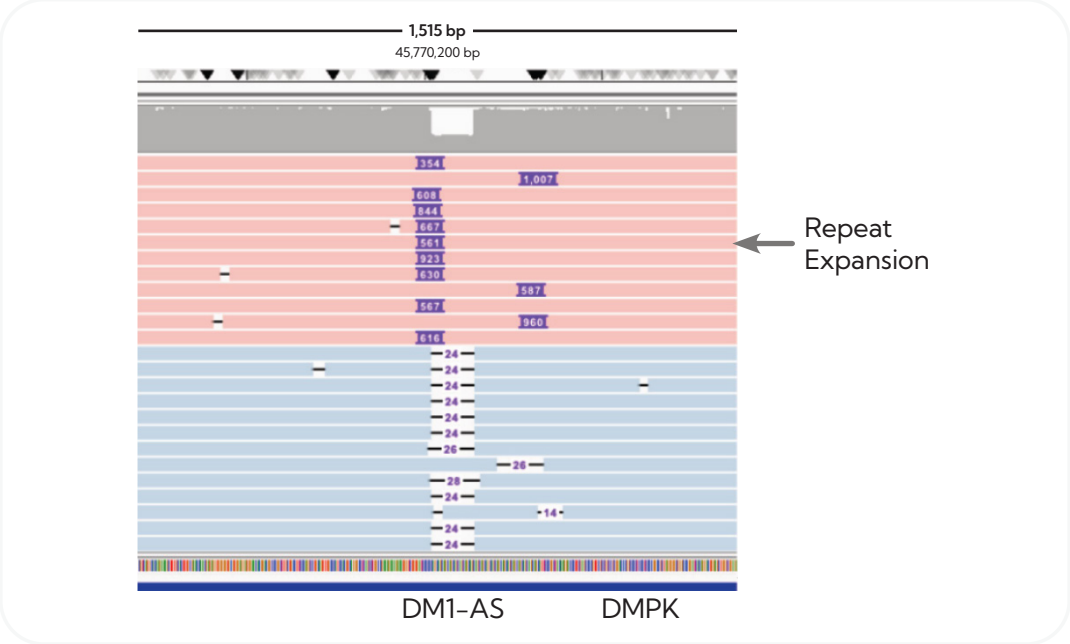
Following negative panel results from a different lab, MyOme Rare Disease Genome Analysis—integrated with confirmatory long-read sequencing— was performed, which identified a diagnostic *DMPK* tandem repeat expansion (TRE) that standard repeat analysis panel had missed. This enabled a molecular diagnosis of myotonic dystrophy 1 (DM1), enabling tailored clinical monitoring and management (**Fig. 8**).

How MyOme Genome and Exome Analyses Integrate Long-Read Sequencing to Improve Performance

Traditional gene panels may miss repeat expansions by detecting only the shorter, healthy allele. Standard short-read WGS lacks the read length to span full repeat expansions, preventing precise determination of expansion boundaries and total copy number. The resulting "positive/negative" result lacks precise repeat counts, making it difficult to interpret disease severity.

MyOme overcomes these limitations by automatically integrating long-read sequencing (LRS) — capable of generating reads >10-100kb — when a TRE is suspected. In this case, short-read WGS flagged a potential *DMPK* expansion, triggering LRS, which resolved a pathogenic, ≥50 CTG repeat associated with DM1—all within a single order (**Fig. 9**).

Fig 9. MyOme Genome Analysis with integrated LRS resolves a diagnostic DMPK expansion.



With MyOme's platform, LRS is also triggered upon detection of certain methylation-associated variants. By characterizing specific methylation signatures, LRS provides insights that can help resolve or confirm certain diagnoses.

MyOme Genome and Exome Analyses outperform targeted repeat panels and traditional short-read WGS tests by integrating LRS:

- **Absolute Resolution of Large Expansions:** LRS produces single, continuous reads that span the full TRE, providing precise read counts.
- **Detection of Stabilizing Interruptions:** The clinical severity of certain TRE disorders is modified by small changes in the repeat sequence.
- **Definitive Haplotype Phasing:** LRS resolves the parental origin of heterozygous TREs, which can influence disease severity.

A comparative summary is presented in **Table 3.**

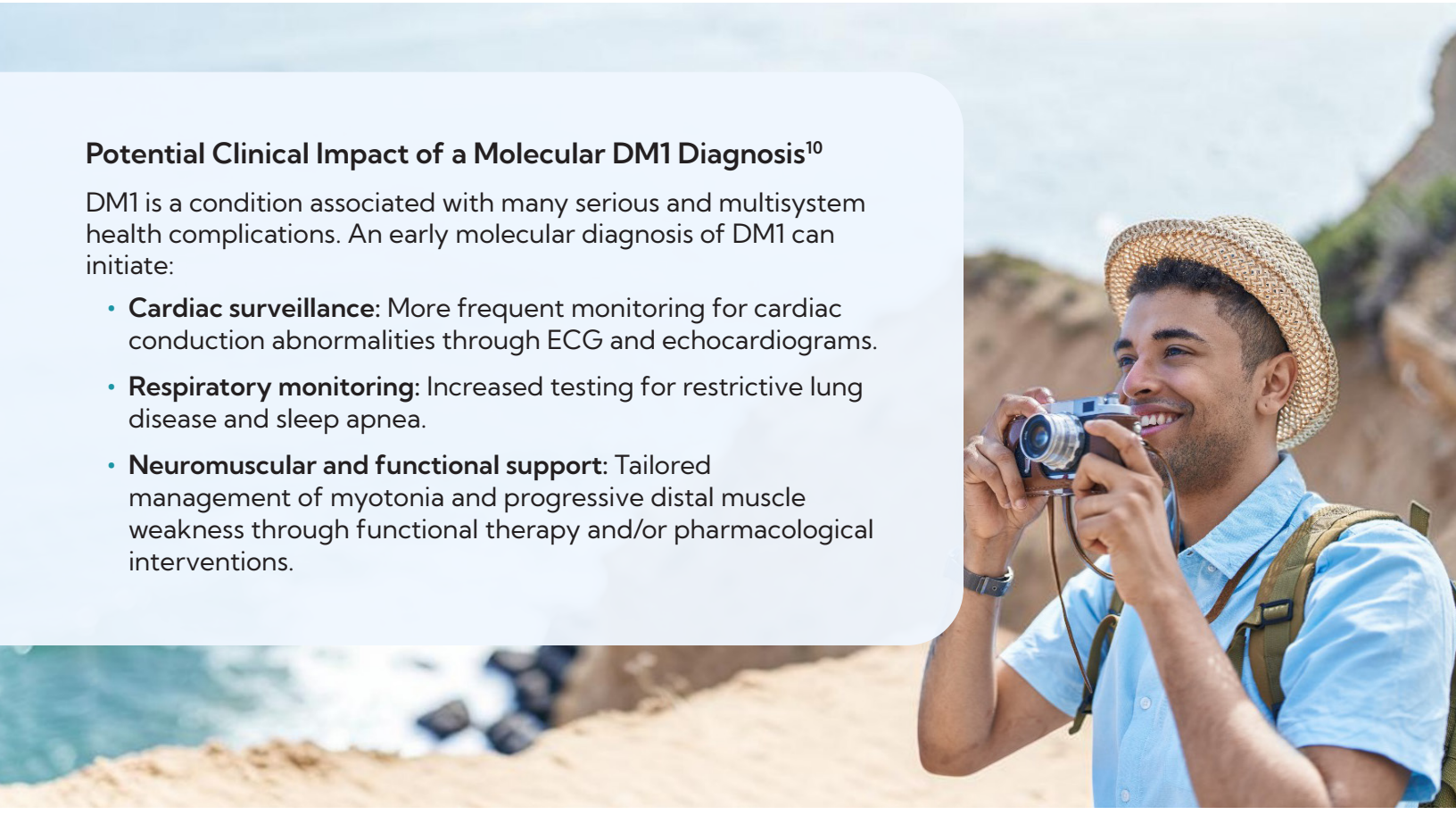
Table 3. TRE Resolution: Gene Panels vs. Short-Read WGS vs. MyOme LRS.

	Gene Panels	Short-Read WGS	MyOme LRS
Allele coverage	Often only healthy allele	Partial coverage of expansion	Full expansion
Readout	Positive/Negative	Positive/Negative	Exact repeat count and size
Stabilizing Interruptions	Not detected	Sometimes detected	Always detected
Phasing	No information	Some information	Definitive information

Potential Clinical Impact of a Molecular DM1 Diagnosis[10]

DM1 is a condition associated with many serious and multisystem health complications. An early molecular diagnosis of DM1 can initiate:

- **Cardiac surveillance:** More frequent monitoring for cardiac conduction abnormalities through ECG and echocardiograms.
- **Respiratory monitoring:** Increased testing for restrictive lung disease and sleep apnea.
- **Neuromuscular and functional support:** Tailored management of myotonia and progressive distal muscle weakness through functional therapy and/or pharmacological interventions.



myome® | Rare Disease

Testing Made Faster, Easier, and More Supportive

Genetic diagnosis can change lives by tailoring monitoring and care, reducing unnecessary interventions, and offering access to support networks. In addition to increasing diagnostic yield, MyOme's genome-first platform was designed to reduce time-to-diagnosis, administrative friction, and overall costs by offering:

Easy Upgrade Workflows:

- Seamlessly upgrade to broader analysis without requiring new appointments, samples, or insurance authorizations.
- Start with insurance-covered CNV or Exome analysis and upgrade affordably to Genome when clinically appropriate.
- Streamline handoff when primary care initiates testing and specialists upgrade analysis as needed.

Enduring Results and Support:

- Receive optional secondary and incidental findings based on informed consent.
- Reanalyze genomic data when new scientific discoveries or updated clinical information emerge.
- Enhance patient understanding and guide next steps with embedded genetic counseling.

Cost-Effective Billing Models:

- Make testing affordable for ~90% of American families with sliding-scale discounts through **MyOme Access**.
- Bill insurance—including commercial insurance, Medicaid, and Medicare—with no delays to testing and prior authorization handled by MyOme.
- Empower patients with flexible payment options, including transparent cash pricing, prompt-pay discounts, and interest-free repayments.

View our Rare Disease **Patient Brochure.**

View our Rare Disease **Billing Brochure.**

References

1. National Organization for Rare Disorders (NORD). Rare disease facts and statistics. Accessed April 1, 2026. https://rarediseases.org/understanding-rare-disease/rare-disease-facts-and-statistics.
2. Huang QQ, Wigdor EM, Malawsky DS, et al. Examining the role of common variants in rare neurodevelopmental conditions. Nature. 2024;636(8042):404–411. doi:10.1038/s41586-024-08217-y.
3. Gorini F, Coi A, Mezzasalma L, Baldacci S, Pierini A, Santoro M. Survival of patients with rare diseases: a population-based study in Tuscany (Italy). Orphanet J Rare Dis. 2021;16(1):275. Published 2021 Jun 14. doi:10.1186/s13023-021-01907-0.
4. Manickam, Kandamurugu, et al. "Exome and genome sequencing for pediatric patients with congenital anomalies or intellectual disability: an evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG)." Genetics in Medicine 23.11 (2021): 2029–2037.
5. Smith, Lacey, et al. "Genetic testing and counseling for the unexplained epilepsies: an evidence - based practice guideline of the National Society of Genetic Counselors." Journal of Genetic Counseling 32.2 (2023): 266–280.
6. Rodan L, Stoler J, Chen E, Geleske T. "Genetic Evaluation of the Child With Intellectual Disability or Global Developmental Delay: Clinical Report". Pediatrics. Published online June 23, 2025.
7. Miroševič Š, Khandelwal S, Amerson E, et al. Paving the way toward treatment solutions for CTNNB1 syndrome: a patient organization perspective. Ther Adv Rare Dis. 2025;6:26330040251318355. Published 2025 Feb 12. doi:10.1177/26330040251318355.
8. Meienberg, Janine, et al. "Clinical sequencing: is WGS the better WES?." Human genetics 135 (2016): 359–362.
9. Sajewicz-Radtke U, Łada-Maśko A, Lipowska M, Radtke BM, Lipska-Ziętkiewicz BS, Krempla-Patron K. The role of multidisciplinary diagnostic and therapeutic model of care in Lamb-Shaffer syndrome - case report. J Appl Genet. 2024;65(4):747–755. doi:10.1007/s13353-024-00838-3.
10. Ashizawa T, Gagnon C, Groh WJ, et al. Consensus-based care recommendations for adults with myotonic dystrophy type 1. Neurol Clin Pract. 2018;8(6):507–520. doi:10.1212/CPJ.0000000000000531.