



# Exome and Genome Sequencing

For Rare and Neurodevelopmental Disorders

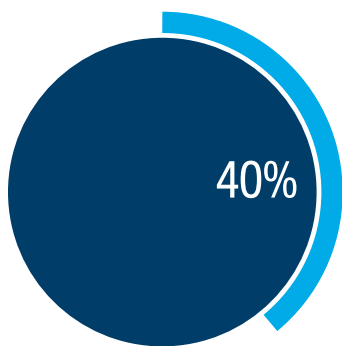


## Help families end the diagnostic odyssey.

Whole exome and whole genome sequencing (WES/WGS) are comprehensive testing approaches recommended for the evaluation of:<sup>1-4</sup>

- Multiple congenital anomalies (MCA)
- Spinal Muscular Atrophy (SMA)\*
- Developmental delay (DD)
- Autism spectrum disorder (ASD)
- Intellectual disability (ID)
- Unexplained epilepsy
- Fragile X syndrome\*
- Cerebral palsy (CP)

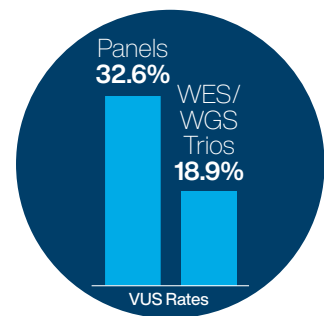
## Genomic testing first: Higher Yield. Fewer Uncertain Results.



Up to 40% of patients will have diagnostic results from genome testing compared to 15-20% from chromosomal microarray<sup>5</sup>



WES and WGS are recommended first-tier diagnostic tests for patients with epilepsy, intellectual disability, developmental delay, and multiple congenital anomalies<sup>1,2,6</sup>



WES and WGS have lower rates of **variants of uncertain significance (VUS)** results compared to panel testing<sup>7</sup>

# Proactive Reanalysis at No Additional Cost

Exome and genome result interpretation depends on our current understanding of gene-disease relationships and variant classifications, and new discoveries are made every month. Through our Patient for Life™ program, our team proactively identifies new discoveries, reviews exome and genome results, and notifies clinicians about new diagnostic findings—indefinitely and at no additional cost.

## How Patient for Life Works:



### 1. Research Review

Ambry's clinical scientists review the latest findings on gene-disease relationships and updates to variant classifications.



### 2. Continuous Reanalysis

Patients' data are continuously analyzed based on new scientific findings.



### 3. Revised Reporting

Ordering providers receive a fully updated report detailing the reclassification and outreach from a genetic counselor.

## Increased diagnostic yield

→ 1 in 20

5% of patients who initially test negative on exome or genome will have a diagnosis identified later through Patient for Life<sup>8</sup>

## We do the work for you

With Patient for Life, reanalysis is always on for new gene-disease associations and variant classifications. Therefore, you don't need to request a reanalysis in most cases.

Manual reanalysis requests are helpful if there are major phenotypic changes in the patient—new signs and symptoms that could provide clues to a diagnosis.

## Equitable access to genetic discovery



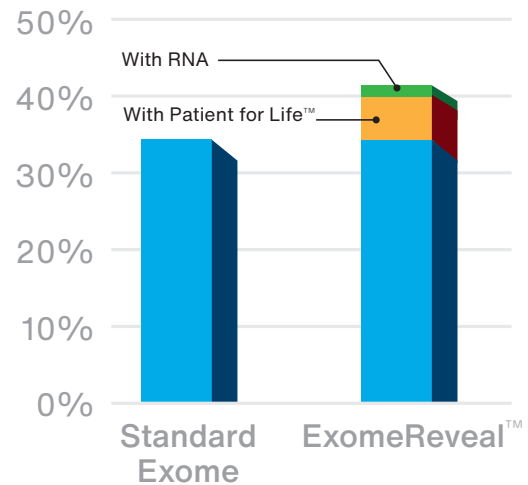
Healthcare disparities related to race and ethnicity have historically influenced access to genetic testing follow-up and reanalysis, particularly when dependent on provider initiation. Evidence suggests non-White patients may experience lower provider-initiated reanalysis<sup>9</sup>, though all racial, ethnic, and ancestral groups benefit. Ambry's Patient for Life program supports diagnostic equity through a proactive, laboratory-initiated approach that does not depend on patients returning to clinic. Continuously monitoring new gene-disease and variant evidence improves access to updated genomic insights.

# Enhancing Diagnostic Yield with Integrated DNA and RNA Analysis

ExomeReveal® | GenomeReveal™

ExomeReveal and GenomeReveal integrate RNA analysis with DNA sequencing to enhance variant interpretation and diagnostic insight.

- Provides an innovative, multi-omic approach to rare disease evaluation<sup>6</sup>
- Expected to impact 1 in 20 patients<sup>10</sup>
- No additional cost to the patient
- RNA analysis increases the diagnostic yield of exome results by ~3%<sup>11</sup>



## RNA Experience that Matters



10+ years performing RNA analysis and interpreting splice variants



30+ RNA experts in-house at Ambry



Our RNA experts serve on multiple independent variant working groups

+8%









Increase in diagnostic yield from RNA + Patient for Life<sup>6, 8, 12</sup>

## Let us be your trusted partner

All exome and genome tests use Ambry's Classifi® program, a proprietary interpretation engine for gene classification, variant analysis, and reporting. It enables genotype-first analysis, ensuring rare or unexpected findings are considered. Multidisciplinary expert review protects relevant variants that could be filtered out by automation, especially for complex phenotypes, and delivers clear, actionable results.

Ambry  
**Classifi**®

# Advanced Diagnostic Testing for Potentially Life-Changing Answers

	ExomeNext®	GenomeNext™
 Proband, Duo, Trio (preferred)	✓	✓
 Turnaround time	3-6 weeks	5-7 weeks
 Blood, saliva, buccal sample	✓	✓
Additional Analysis		
 RNA analysis (blood sample required)*	ExomeReveal® (optional)	GenomeReveal™ (optional)
 Patient for Life™	✓	✓
 Mitochondrial genome	Optional	✓
 ACMG Secondary Findings	Optional	Optional
 Short tandem repeats (STRs)**		✓

\* Requires EDTA (DNA) and PAXgene (RNA) specimens. Reported 3-4 weeks after initial DNA results

\*\* See website for current list of STRs included in WGS.

## References:

- Manickam K 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). Genet Med. 2021;23(11):2029-37. doi: 10.1038/s41436-021-01242
- Smith L et al. Genetic testing and counseling for the unexplained epilepsies: An evidence-based practice guideline of the National Society of Genetic Counselors. J Genet Couns. 2022 Oct 24. doi.org/10.1002/jgc4.1646
- Srivastava S et al. Meta-analysis and multidisciplinary consensus statement: Exome sequencing is a first-tier clinical diagnostic test for individuals with neurodevelopmental disorders. Genet Med. 2019 Nov;21(11):2413-21; https://doi.org/10.1038/s41436-019-0554-6
- Srivastava S et al. Molecular diagnostic yield of exome sequencing and chromosomal microarray in cerebral palsy: A systematic review and meta-analysis. JAMA Neurol. 2022 Dec 1;79(12):1287-1295. doi: 10.1001/jamaneuro.2022.3549
- Wojcik MD, Lemire G, Berger E, et al. Genome Sequencing for Diagnosing Rare Diseases. N Engl J Med. 2024 Jun 6;390(21):1985-1997. doi:10.1056/NEJMoa2314761
- Rodan LH, Stoler J, Chen E, et al. Genetic Evaluation of the Child With Intellectual Disability or Global Developmental Delay: Clinical Report. Pediatrics. 2025 Jul 1;156(1):e2025072219. doi:10.1542/peds.2025-072219
- Rehm et al. The landscape of reported VUS in multi-gene panel and genomic testing: Time for a change. Genet Med. 2023 Jul 30;25(12):100947. Doi: 10.1016/j.gim.2023.100947.
- Towne MC, et al. Impact of laboratory-driven proactive reanalysis: Reclassification to positive in 5% of initially negative or uncertain exome sequencing cases. Genet Med. 2025;27(9):101464. doi:10.1016/j.gim.2025.101464
- Giles A, et al. 10 years of exome sequencing and reanalysis among racial, ethnic, and ancestral groups: the importance of equitable reanalysis access. Genet Med. 2025 Oct 16:101576. doi:10.1016/j.gim.2025.101576. Ambrly internal data.
- Ichikawa S, Yergert K, Gasser B, Towne MC, Burow D. Utility of Targeted RNA Analysis in Neurogenetic Disorders. Neurol Genet. 2026;12(2):e200341. Published 2026 Feb 20. doi:10.1212/NXG.000000000200341
- Ambrly Genetics, Medical Affairs. Emerging evidence from ExomeReveal™ Early Access Program. Unpublished internal data. 2024
- Horton C, Cass A, Conner BR, et al. Mutational and splicing landscape in a cohort of 43,000 patients tested for hereditary cancer. NPJ Genom Med.2022;7(1):49. Published 2022 Aug 25. doi:10.1038/s41525-022-00323-y