REFERENCE GUIDE

Ambry Genetics®
A TEMPUS COMPANY

ExomeNext®
ExomeReveal®

Genetic Testing for Rare Disease and Neurodevelopmental Disorders

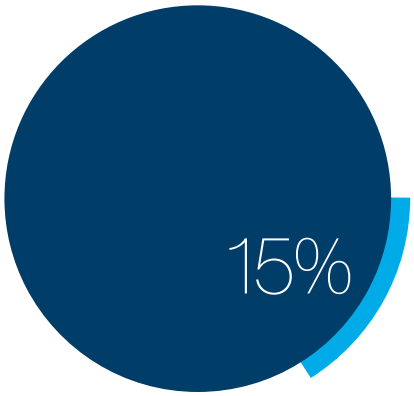
Help families end the diagnostic odyssey.

Whole exome sequencing (WES) is a comprehensive testing approach recommended for the evaluation of:[1–4]

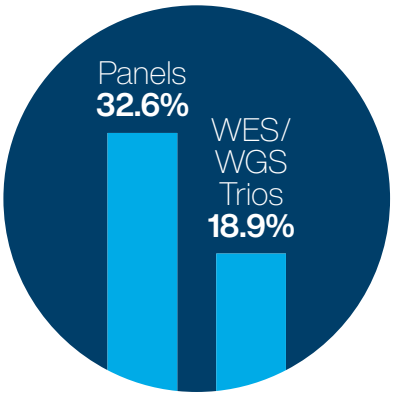
- Multiple congenital anomalies (MCA)
- Developmental delay (DD)
- Intellectual disability (ID)
- Autism spectrum disorder (ASD)
- Unexplained epilepsy
- Cerebral palsy (CP)

Exome first: More answers. Clearer results.

Up to 1 in 3 patients will have diagnostic results from exome testing compared to 15–20% from chromosomal microarray[3]



Additional findings on exome that would have been missed by panel testing[5]



Lower rates of variants of uncertain significance (VUS) in exome/genome[6]

Proactive Reanalysis at No Additional Cost

All exome sequencing tests depend 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 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 will have a diagnosis identified later through Patient for Life[7]

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 because of race and ethnicity impact genetic testing. Our data show that African American/Black patients were consistently left behind in exome testing, with lower diagnostic yields and provider-initiated reanalysis rates. However, they were most likely to have a reclassification when reanalysis was performed.[8] Patient for Life ensures equitable access to new diagnostic information.

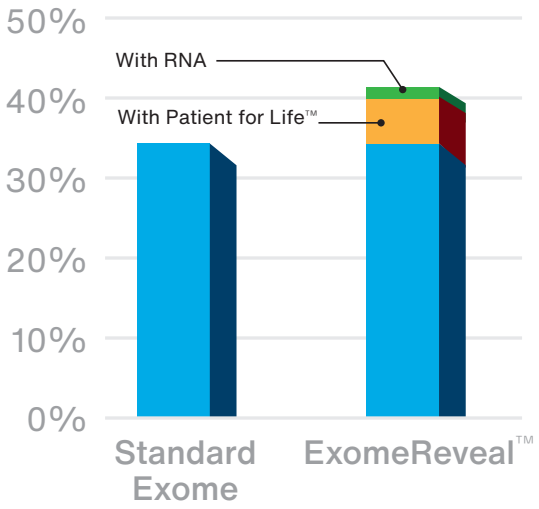
Maximize the Diagnostic Yield Over Standard Exomes

Introducing

ExomeReveal®

ExomeReveal adds the power of RNA analysis to exome testing.

- Provides an innovative, multi-omic approach to rare disease
- Expected to impact 1 in 50 patients[10]
- No additional cost to the patient



+20% Increase in diagnostic yield compared to standard exomes when combined with Patient for Life[7, 9, 10]

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

Let us be your trusted partner

All exome tests utilize Ambry's Classifi® program, a proprietary, knowledge-driven engine for gene classification, variant analysis & interpretation, and reporting. The Classifi program delivers the highest quality test results and ensures we leave no stone unturned in getting answers for you and your patients.

Ambry Classifi®

Advanced Diagnostic Testing for Potentially Life-Changing Answers

ExomeNext®

PREFERRED

Trio
(with both parents)

ACCEPTABLE

Duo
(with one parent)

Proband Only

3–6 weeks turnaround

Blood, saliva and buccal samples accepted

ExomeReveal®

RNA analysis performed for eligible DNA variants expected to impact splicing.

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

Did you know?

Ambry was the first commercial lab to offer whole exome sequencing in 2011.

Technical Test Performance

- >97% of the exome covered with a minimum depth of coverage of 20X
- Detects gross deletions and duplications ≥5 exons
- Within mitochondrial DNA, >5% heteroplasmy is detected

References:

1. 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
2. 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
3. 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
4. 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/jamaneurol.2022.3549
5. Schultz C et al. Consider the net you cast: Multigene panel testing misses 15% of diagnostic results compared to exome sequencing. Poster presented at: Child Neurology Society conference; October 2023; Vancouver, BC, Canada.
6. 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.
7. 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
8. 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
9. Ambry internal data.
10. 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

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