REFERENCE GUIDE

Ambry Genetics®

ExomeNext® ExomeReveal™

Genetic Testing for Rare Disease and Neurodevelopmental Disorders

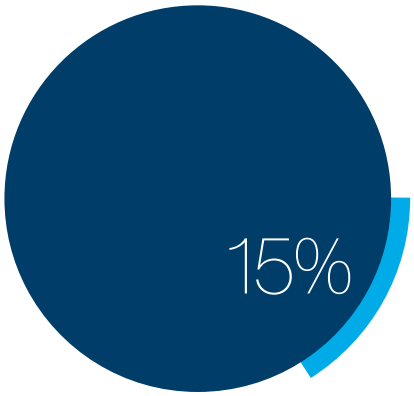
Help families end the diagnostic odyssey.

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

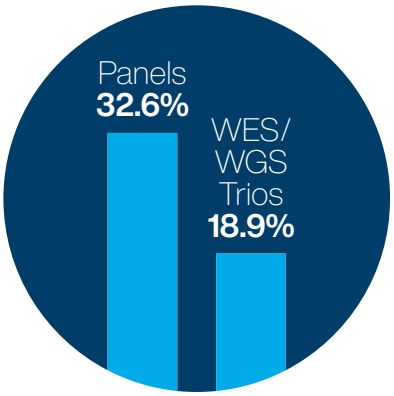
- Multiple congenital anomalies (MCA)
- Developmental delay (DD)
- Intellectual disability (ID)
- Autism spectrum disorder (ASD)
- Unexplained epilepsy
- Cerebral palsy (CP)

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 updates to the family history or 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.

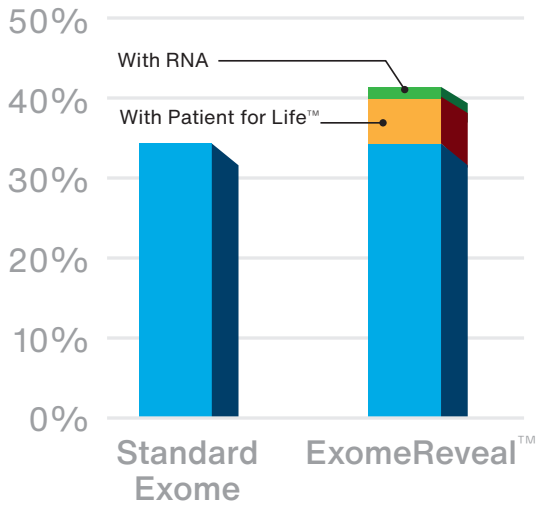
Maximize the Diagnostic Yield Over Standard Exomes

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

8+ 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

6–8 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:

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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. Smith ED et al. Classification of genes: Standardized clinical validity assessment of gene-disease associations aids diagnostic exome analysis and reclassifications. *Hum Mutat.* 2017 May;38(5):600-608. doi: 10.1002/humu.23183.
8. Giles A et al. Addressing equity in exome sequencing: Proactive reanalysis helps to reduce racial, ethnic and ancestral disparities. Platform presented at: National Society of Genetic Counselors conference; October 2023; Chicago, IL, USA.
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