Ambry Genetics®

ExomeNext®

Reference Guide

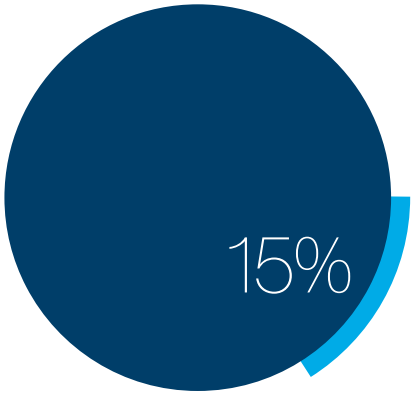
Help families end the diagnostic odyssey.

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

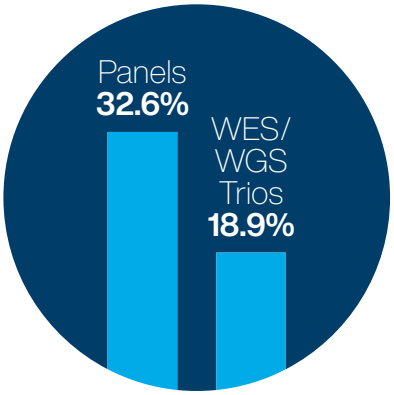
- Multiple congenital anomalies (MCA)
- Developmental delay (DD)
- Intellectual disability (ID)
- Autism spectrum disorder (ASD)
- Unexplained epilepsy
- Cerebral palsy (CP)

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 new discoveries are made every month. Through our Patient for Life program, our team proactively identifies new discoveries, reviews exome results, and proactively 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

2. REANALYSIS

Patients' exome data are reanalyzed, and reclassification reports are issued for new, clinically-relevant genes

3. REVISED REPORTING

Ordering providers are provided a reclassification report proactively and at no additional cost

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. 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.

Patient for Life Case Study

A Journey from Uncertainty to Potential Therapy

2019

A Family in Need of Answers

An infant presents to neurology with severe epileptic encephalopathy, lower extremity spasticity and severe cognitive delays.

Exome Testing Uninformative

ExomeNext testing is initially negative, although two suspicious variants were identified in an uncharacterized gene, *HPDL*.

2020

New Data, New Answers

An AJHG publication identifies *HPDL* as type of autosomal recessive spastic paraplegia.

Results Updated via Patient for Life

The *HPDL* gene was reclassified by the Ambry team and a new ExomeNext report was issued, confirming a diagnosis for the patient.

2023

Hope for Treatment

Researchers at the University of San Diego initiate a clinical trial testing potential therapy 4-hydroxymandelate, required for the synthesis of coenzyme Q10.

Expert Support is Always in Reach

Ambry's team of Genomic Science Liaisons contact you directly with Patient for Life results.

They are also available for clinical education, product consultation, and other test support.

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™

Unparalleled Access to 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

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

Did you know?

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

Excellent Coverage. Personalized Support.

In-network: Ambry is contracted and in-network with the majority of US health plans, and many plans cover genetic testing.

Transparent: We review cases for alignment with payer policy and handle prior authorization (where permitted). We communicate cost estimates up-front with patients and do not balance bill.

Committed to access: We offer patient-pay pricing and patient assistance when there is financial need.

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. 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.
9. Ambry internal data.

Ambry Genetics®

One Enterprise, Aliso Viejo, CA 92656 USA Toll Free +1.866.262.7943 Fax +1.949.900.5501 **ambrygen.com**

MKT-SPEC-BRO-50004-EN v11 10.11.23