Ambry Genetics®
A Konica Minolta Company

ExomeNext

REFERENCE GUIDE

June 2018

Finding Answers with Diagnostic Exome Sequencing (DES)

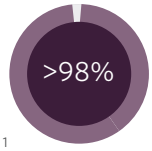
An undiagnosed condition is a painful and heart-breaking journey. ExomeNext is the first clinically-available whole exome sequencing platform that leverages the power of trio data, a unique inheritance-based bioinformatics filtering pipeline, and robust data curation to bring an end to the diagnostic odyssey experienced by more than one-third of previously undiagnosed patients.

EXCELLENT COVERAGE

Excellent coverage across the entire genome

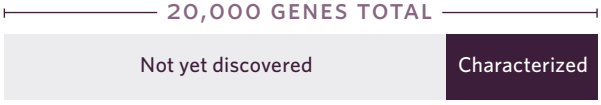
>95% of the exome covered with a minimum depth of coverage of 20X

EXOME VS. PANELS
Exome detection mirrors panels. >98% of point mutations found on panels also identified by ExomeNext.[1]



LEADERS IN EXOME ANALYSIS

First published criteria for assessing clinical validity of gene-disease relationships[2]



Of the 20,000 genes, only ~5,000 have been characterized. Ambry is leading the efforts to define these genes for the community.

IDENTIFY MORE PATIENTS

Identify 8% more with our validated candidate gene analysis[3,4]

**Diagnostic rates vary based on test ordered. Trio test options provide ~2x higher detection rates than proband only.*

PATIENT FOR LIFE

ExomeNext doesn't end with the initial report. Ambry's ongoing internal reanalysis program is included with every ExomeNext. Clinicians are notified if the efforts identify an answer for their patient.

DATA SHARING + COLLABORATIONS + ONGOING INTERNAL RE-ANALYSIS + PHYSICIAN REQUESTED RE-ANALYSIS

6% overall reclassification

Why Ambry

Most Experienced
1st to launch clinical exome (2011)

2011

2015

Ending Diagnostic Odyssey
Highest published diagnostic yield[3]

Evidence-Based Reporting
1st to publish algorithm for candidate (novel) gene reporting[4]

2016

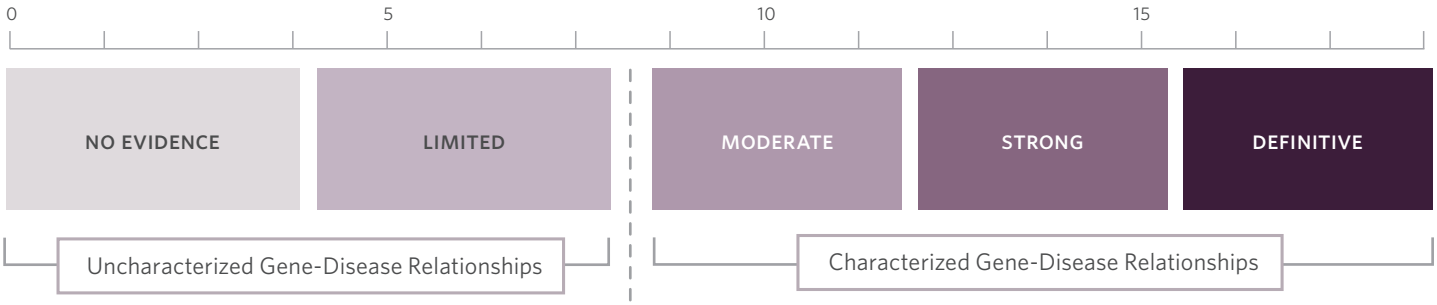
2017

Evidence-Based Analysis
First established scoring system for gene classification and clinical-validity assessment[2]

Evidence-Based Analysis

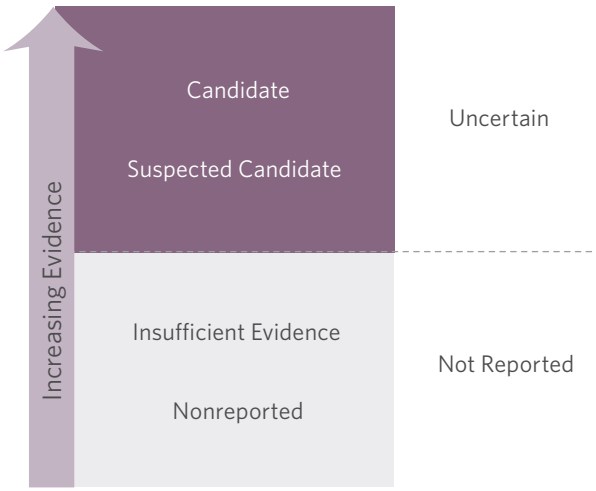
ExomeNext follows an evidence-based analysis and reporting model. All reporting is phenotype-driven and focused on reporting findings related to the patient's clinical presentation.[2-4]

1. Gene Classification



2. Clinical Correlation

CANDIDATE GENE REPORTING CRITERIA[4]



ACMG-BASED REPORTING CRITERIA

CATEGORIZATION OF CHARACTERIZED GENETIC ETIOLOGIES		
Clinical Correlation	Alteration Classification	Overall Results Category
Positive	Pathogenic	POSITIVE
	Likely Pathogenic	LIKELY PATHOGENIC
	Uncertain	UNCERTAIN
Likely Positive	Pathogenic	LIKELY POSITIVE
	Likely Pathogenic	LIKELY POSITIVE
	Uncertain	UNCERTAIN
Uncertain	Likely Positive	UNCERTAIN
	Likely Pathogenic	UNCERTAIN
	Uncertain	UNCERTAIN

Test Options

FLEXIBLE AND COMPREHENSIVE TESTING OPTIONS

	EXOMENEXT-*PROBAND*	EXOMENEXT-*TRIO*	EXOMENEXT-*RAPID**	EXOMENEXT-*SELECT*
Turnaround time	6-8 weeks	6-8 weeks	8 days**	3-5 weeks
Number of genes analyzed	~5,000	Up to ~20,000	Up to ~20,000	Up to 500
Mitochondrial genome	Optional	Optional	Included	No
Number of individuals sequenced	1	3	3	1
Co-segregation analysis	Included	Included	Included	Included
Secondary Findings Results	Included	Included	Included	No

** Only institutional and cash billing are accepted*

*** Verbal result provided within 8 days when an informative trio is provided; full report including mtDNA analysis, co-segregation analysis, and Sanger confirmation provided within 14 days.*

How to Order

SIMPLE ORDERING PROCESS

ACCEPTED SPECIMENS: Proband and Family Members: Blood, Saliva, DNA

1

ORDER SUBMISSION

a. Proband specimen
b. Family Member specimens (Required for Trio orders)
c. Clinic Notes
d. Medical Necessity Form (insurance orders)

2

ORDER REVIEW

a. Required documents & samples
b. Test authorization (insurance orders)

3

AMBRY BEGINS TESTING

4

RESULT AVAILABLE IN 6-8 WEEKS

Results available through mail, fax, or online portal.

REFERENCES

1. LaDuca H, *et al.* Exome Sequencing covers >98% of mutations identified on targeted next generation sequencing panels. PLoS One. 2017 Feb 2;12(2).
2. Smith ED, *et al.* Classification of genes: Standardized clinical validity assessment of gene-disease associations aids diagnostic exome analysis and reclassifications. Hum Mutat 2017 Jan 20. [Epub ahead of print.]
3. Farwell KD, *et al.* Enhanced utility of family-centered diagnostic exome sequencing with inheritance model-based analysis: results from 500 unselected families with undiagnosed genetic conditions. Genet Med. 2015 Jul:17(7): 578-86.
4. Farwell Hagman KD, *et al.* Candidate-gene criteria for clinical reporting: diagnostic exome sequencing identifies altered candidate genes among 8% of patients with undiagnosed diseases. Genet Med. 2017 Feb;19(2):224-225.

Over 1 Million Tests Completed

MOVING SCIENCE FORWARD

Purposeful Confirmatory Testing

Many labs validate their tests based on certain limited studies. That's why we participated and led the largest study of its kind (20,000 cases) guiding us to utilize confirmatory testing when we see specific well-defined thresholds. Our mission is to get it right the first time.

Understanding Disease Better Through Free Data Sharing

Identifying an individual's genetic information is nothing new—it's what we do with it that is unique. When labs share genomic information, we can together accelerate the understanding of human disease. Through AmbryShare, we leverage de-identified information to collaborate with others and help people everywhere find answers.

SuperLab

Our 65,000 square foot highly-automated CLIA/CAP certified lab produces some of the fastest turnaround times in the industry, without compromising testing accuracy or specificity.

Ambry's Translational Genomics (ATG) Lab

As an advanced diagnostic lab, it's our responsibility to ensure the results you get from us are accurate and that classification is as complete and robust as possible. Our ATG lab is a unique laboratory that provides an additional service at no additional cost for you and your patients to generate more precise data potentially bringing clarity to some variants of unknown significance (VUS). This helps to actively drive down the rate of VUS results and can give you an increased understanding of your patient's results, so you can better provide medical management recommendations and improve health outcomes.

About Ambry

By identifying an inherited condition early on with genetic testing, we are given a chance to get in front of the disease with timely intervention instead of treating it after it has taken root with expensive therapies, potentially impacting quality of life. The more information we have earlier on; the more choices we have to make timely actionable, value-based healthcare decisions.

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