Ambry's *BRCA1/BRCA2* Test Information

ANALYTIC SENSITIVITY	> 99.97%	Ambry's *BRCA1/2* analytic sensitivity and specificity is greater than 99.97% for thousands of samples tested for described mutations.
VUS RATE	4.4%	Our current combined *BRCA1/2* VUS rate is 4.4%. We update and post our VUS rate at brcaandbeyond.com and are committed to transparency.
CLASSIFICATION CONFIDENCE	> 99%	Ambry follows the ACMG (American College of Medical Genetics) and IARC (International Agency for Research on Cancer) variant classification recommendations (Richards CS *et al*., Genet Med, 2007; Plon SE *et al*, Hum Mutat, 2008).
SEQUENCING TECHNOLOGY	NGS	Our *BRCA1/2* sequencing uses next generation sequencing (NGS) technology. NGS carries out the sequencing process in millions of reactions through massively parallel sequencing to achieve enhanced resolution, throughput and speed. All reported VUSs and mutations are Sanger confirmed.
TARGET ENRICHMENT	PRIMER TILING	Our unique custom primer tiling design provides amplicon redundancy which significantly reduces allele dropout leading to false negatives (allele dropout is more common with sequencing assays that use one primer pair per exon).
BASE PAIR COVERAGE	10,000X	Ambry's average NGS sequence coverage for *BRCA1/2* is greater than 10,000X – thousands of times greater than Sanger-based assays where a typical base is only covered at 2X with a forward and reverse sequence read.
INTRON COVERAGE	OPTIMIZED	Ambry's approach to peri-exonic regions maximizes sensitivity while limiting the reporting of intronic variants, nearly all of which are benign polymorphisms. Our test sequences deep into the introns. Any previously known *BRCA* mutations are identified, Sanger confirmed and reported, regardless of intronic location. Ambry restricts the reporting of variants (not mutations) to +5 or -5 into the intronic regions.
VARIANT CLASSIFICATION	ROBUST	We utilize a 5-tier variant classification system incorporating multiple lines of evidence, including: ACMG Guidelines, IARC variant classifications recommendations, thorough literature review, general population frequency, co-occurrence data, co-segregation data, conservation data, and *in silico* analysis tools. Ambry provides a detailed result definition that clearly delineates the various levels of evidence for each mutation, variant likely pathogenic and variant of unknown significance (VUS).
DELETION/ DUPLICATION TECHNOLOGY	CUSTOM TARGETED MICROARRAY	Ambry has offered clinical microarray analysis since 2009, first applying genome-wide (chromosomal) arrays to the pediatric market. For other tests, such as our hereditary cancer panels, we have custom designed a gene specific targeted microarray, optimizing this technology to identify gross deletions/duplications. Our custom tiled array (aCGH) averages 10 probes per exon, covers promoter and intronic regions, and is sensitive enough to pick up partial and single exon deletions. Even smaller deletions, including those under 75 bp, are detected via our NGS sequencing pipleline. For *BRCA1/2* testing performed alone, MLPA is used to detect gross deletions/duplications.
# OF VARIANTS DEPOSITED	> 16,000	Ambry will routinely share de-identified *BRCA1/2* data with research collaborators and public databases. We made our first deposit into the BIC database on July 30, 2013, making us the first commercial US lab to contribute data since 2006.

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Ambry Genetics™

BRCA1/BRCA2 Test Logistics

INSURANCE PRE-VERIFICATION	YES	Ambry performs pre-verification with and without samples. We are contracted with the majority of commercial insurance companies and Medicare. All out-of-network patients are treated as in-network to minimize out of pocket costs. We work with the majority of Medicaid plans and most require pre-verification.
OUT-OF-POCKET NOTIFICATION	$100	If patient out-of-pocket financial responsibility is potentially greater than $100, Ambry will contact the patient for verbal approval prior to initiating the test.
PRICE	$2200	This price includes sequencing and deletion/duplication testing. Ambry is committed to improving patient access to medically necessary genetic testing. Our institutional list price reflects this commitment.
AVERAGE TAT	14 DAYS	Our quoted turn-around-time is 14-21 days. The average TAT is 13.9 days currently and is decreasing.
TEST OPTIONS	MULTIPLE	*BRCA1/2* sequencing with deletion/duplication, specific site analysis for known mutations, Ashkenazi Jewish 3-mutation panel. Also included in cancer panels: *BRCA*plus, BreastNext, OvaNext, PancNext, CancerNext.
ELECTRONIC ORDERING	AP2.0	AmbryPort 2.0 (AP2.0) is a functional and easy to use HIPAA compliant document exchange system. It is designed to function as an all-encompassing client portal equipped with test ordering, pre-verification capabilities, sample tracking and ability to download/print test reports.

Next-Generation Sequencing Expertise

- In 2007, Ambry was one of the first commercial labs to invest in NGS technology.
- Ambry was the first lab to introduce NGS into the clinical setting with the launch of an 81-gene panel (2010).
- In early 2012, Ambry was the first commercial lab to offer multi-gene hereditary cancer panels and is the most experienced lab with cancer panel tests. Our current cancer panel menu includes: *BRCA*plus, BreastNext, ColoNext, OvaNext, PancNext, PGLNext, RenalNext and CancerNext. These panels range from 6-28 genes.
- To date, we have analyzed more than 20,000 diagnostic and more than 100,000 total NGS samples.

About Ambry Genetics

- Offering clinical genetic testing since 2001
- CAP-accredited and CLIA-certified diagnostic laboratory
- We hold the required state licenses including California and New York Clinical Laboratory licenses
- Comprehensive test menu of more than 300 different genes
- World-wide leaders in hereditary cancer testing with the largest cancer test menu (75 genes) in North America
- Genetic counselors and medical directors are readily available to assist in test selection, case reviews, and result interpretation

Since 2001, Ambry has performed hundreds of thousands of genetic tests and identified more than 45,000 mutations in greater than 500 different genes.

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