Transform carrier screening research with the CarrierScan Assay

Background

Advances in genetic analysis tools are revolutionizing reproductive health and transforming the way carrier screening research is being conducted. Traditionally, molecular research laboratories have focused on analyzing just a few genetic changes that cause inherited diseases, and are known or assumed to be associated with an individual's ethnicity. With the identification of more causative variants—both sequence and structural—and increasing ethnic diversity in certain regions, it is becoming significantly important to expand carrier screening research to include more variants and diseases.

The Applied Biosystems™ CarrierScan™ Assay is an innovative, comprehensive, and high-throughput microarray-based tool for the reliable and robust detection of sequence and structural variation for preconception expanded carrier screening research across a wide range of ethnicities. The unique feature of this tool is the ability to consolidate multiple copy number and genotyping tests into a single molecular assay. With simple data analysis and reporting software included in the complete solution, high-throughput molecular labs can generate all relevant carrier screening research data quickly.

Key benefits for molecular research laboratories:

- **Increase productivity and efficiency**—save time and costs by replacing multiple tests with a single assay
- **Trust in your results**—gain confidence in your data with an assay that uses empirically selected probes and has been biologically verified for the most common markers
- **Analyze and report data with ease**—quickly and intuitively translate data into results, customizing export formats with Applied Biosystems™ CarrierScan™ Reporter Software
- **Run more samples and reduce hands-on time**—process 96 samples per run, up to 768 samples per week with the flexibility of manual or automated sample preparation on the Applied Biosystems™ GeneTitan™ Multi-Channel (MC) Instrument

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The complete CarrierScan Assay solution offers flexibility and scalability to meet the changing needs of high-throughput molecular research labs and includes the following components:

Multiple assays in one

To perform expanded carrier screening research efficiently and reliably, a laboratory must be able to assess a wide range of genetic changes in each sample. For example, complex recessively inherited conditions (Figure 1) such as α- and β-thalassemia can be caused by multiple types of genetic variants including copy number deletions or duplications in either *HBA1*, *HBA2*, or both genes (α-thalassemia), and mutations in the *HBB* gene (β-thalassemia and sickle-cell anemia). For accurate detection of each of these variants, multiple technologies including PCR, multiplex ligation-dependent probe amplification (MLPA), sequencing, and microarrays are needed for comprehensive analysis of a single sample. This extensive requirement may limit a laboratory's potential throughput and may increase infrastructure, maintenance, and labor costs.

Reliable detection of sequence and structural variants in a single assay

The CarrierScan Assay enables detection of both sequence and structural variants simultaneously, including biallelic and multiallelic mutations such as single-nucleotide variants (SNVs), insertion-deletion variants (in-dels), as well as structural genomic variants, such as small intragenic deletions and duplications (copy number variants). This one-stop solution offers a unique opportunity to consolidate the number of assays and technologies required to perform expanded carrier screening research into one, to help save time and costs.

Trust your results with verified content

All detection probes used on the CarrierScan microarray have been empirically selected based on assessment of performance in more than 1,500 samples with variants to enable highly accurate, reproducible, and robust data.

Empirical probe selection enables:

- Reduction of false calls caused by neighboring interfering variants (e.g., the delta F508 mutation on the *CFTR* gene)
- High true variant detection even in challenging regions of sequence homology in pseudogenes (e.g., *GBA* and *ARSA*, among others)

In addition, the most common variants have been technically and biologically verified at multiple independent locations using variant-positive samples—yielding 100% concordant results, and demonstrating excellent robustness and reproducibility. The CarrierScan Assay also offers the flexibility to analyze multiple sample types, including whole blood, tissue, cell lines, and buccal samples with more than a 98% pass rate.

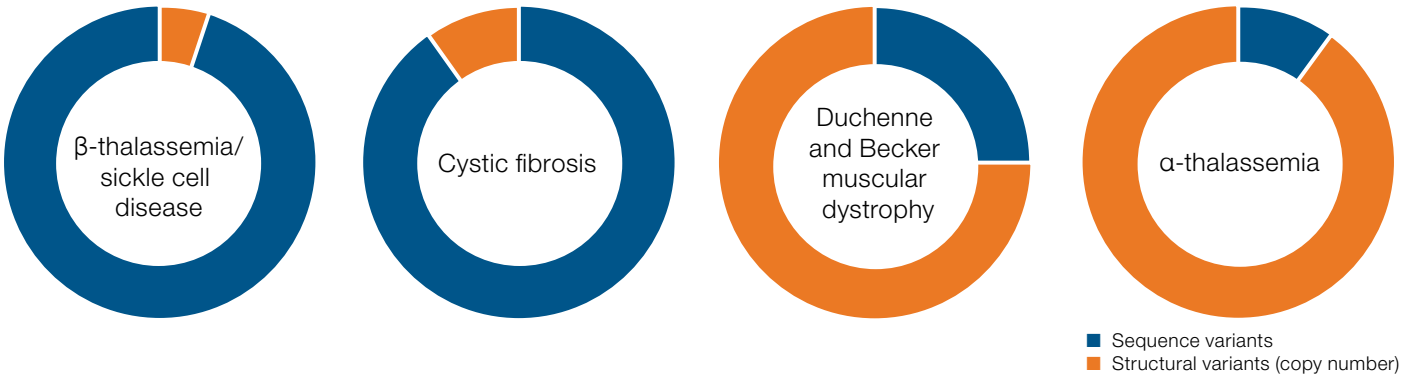

Figure 1. Common genetic conditions requiring detection of both sequence and structural variants.

Comprehensive coverage from the content sources you trust

The CarrierScan Assay detects 6,000 sequence and structural variants in over 600 genes for 600 diseases, informed by the American College of Medical Genetics (ACMG) and the American College of Obstetricians and Gynecologists (ACOG) guidelines from well-curated, prominent databases and peer-reviewed literature [1–6].

Figure 2 shows examples of the comprehensive content offered by the CarrierScan Assay. For the *CFTR* gene, as an example, detection probes are included only for those mutations that are found in databases and for which relevance has been confirmed in published literature. Additionally, exon-level copy number markers are included to increase the sensitivity of the assay. Likewise, for the *DMD* gene, exon-level coverage is achieved with more than 12,000 empirically selected probes for reliable detection of structural variants containing deletions and duplications (del/dups). The comprehensive content also includes optional ancestry-informative markers (AIMs) for population analysis, and probes for sample identity tracking and quality assurance.

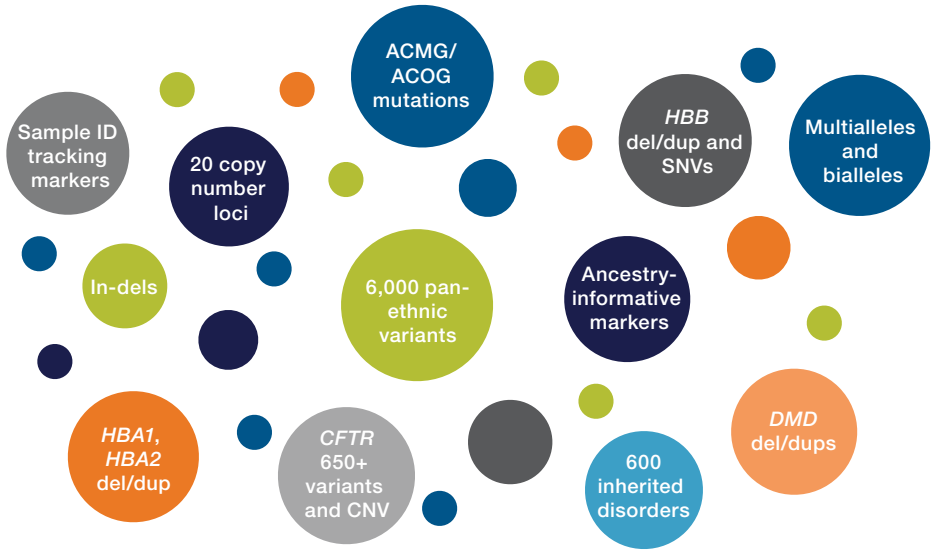

Figure 2. Examples of the comprehensive content included in the CarrierScan Assay.

Simple data analysis and reporting

Powerful biallelic and multiallelic detection, as well as state-of-the-art copy number algorithms are included in CarrierScan Reporter Software and used in conjunction with curated annotations for population frequencies, providing quick, reliable, and automated data analysis.

Additionally, CarrierScan Reporter Software automates the most common calculations for single and paired sample analysis for carrier screening research, making reporting simple. Lastly, export of annotations is customizable by population or panel, allowing you to filter and translate data quickly and easily into a format that meets your specific laboratory needs (Figure 3).

CarrierScan Reporter Software workflow

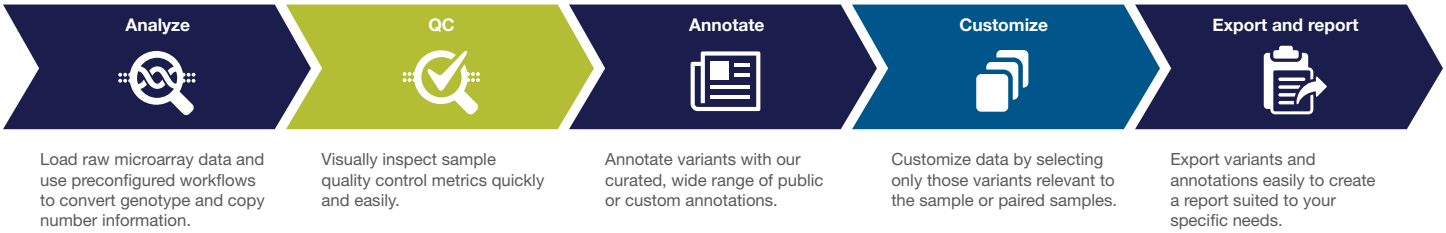

Figure 3. Data analysis workflow steps in CarrierScan Reporter Software.

Transform your lab

Adopt the new CarrierScan Assay to establish efficient, comprehensive, and consolidated expanded carrier screening research in your laboratory.

Gain the advantage and request a consultation today at **thermofisher.com/carrierscan**

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Supporting information

Example content included in the CarrierScan Assay

Disorder	Gene	Sequence variants	Structural variants detection
ACMG and ACOG content			
Cystic fibrosis	*CFTR*	662	Yes
Sickle-cell disorders/β-thalassemia	*HBB*	118	Yes
Tay–Sachs disease	*HEXA*	84	
Bloom syndrome	*BLM*	54	
Canavan disease	*ASPA*	48	
Niemann–Pick disease, type A/B	*SMPD1*	47	
Gaucher disease	*GBA*	30	
Fanconi anemia, complementation group C	*FANCC*	28	
Mucolipidosis IV	*MCOLN1*	14	
α-thalassemia	*HBA1/HBA2*	11	Yes
Familial dysautonomia	*IKBKAP*	3	
Hyperinsulinemic hypoglycemia, familial, 1	*ABCC8*	82	
Glycogen storage disease type Ia	*G6PC*	70	
Glycogen storage disease type Ib	*SLC37A4*	16	
Fanconi anemia, complementation group A	*FANCA*	19	Yes
Fanconi anemia, complementation group G	*FANCG*	9	
Joubert syndrome 2	*TMEM216*	7	
Joubert syndrome 7	*RPGRIP1L*	2	
Maple syrup urine disease, type IA	*BCKDHA*	32	
Maple syrup urine disease, type IB	*BCKDHB*	24	
Maple syrup urine disease, type II	*DBT*	7	Yes

Please contact us for the complete list of genes covered at **thermofisher.com/carrierscan**

References

1. Grody WW et al. (2013) ACMG position statement on prenatal/preconception expanded carrier screening. *Genet Med* 15:482–483.
2. Landrum MJ et al. (2016) ClinVar: public archive of interpretations of clinically relevant variants. *Nucleic Acids Res* 44:D862–868.
3. Stenson PD et al. (2003) Human Gene Mutation Database (HGMD): 2003 update. *Hum Mutat* 21:577–581.
4. Zlotogora J et al. (2015) The Israeli national population program of genetic carrier screening for reproductive purposes. *Genet Med* 18:203–206.
5. Langfelder-Schwind E et al. (2014) Molecular testing for cystic fibrosis carrier status practice guidelines: recommendations of the National Society of Genetic Counselors. *J Genet Couns* 23:5–15.
6. Sosnay PR et al. (2013) Defining the disease liability of variants in the cystic fibrosis transmembrane conductance regulator gene. *Nat Genet* 45:1160–1167.

Find out more at **thermofisher.com/carrierscan**

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