NGS Constitutional Disease Research Solutions

Target Enrichment System

Pave the Way

From Samples to Answers

Agilent Technologies

Agilent NGS: Revolutionizing Clinical Research

Agilent offers a full range of catalog and custom target enrichment solutions that enable a streamlined workflow tailored to meet specific needs for target coverage, throughput and turn-around time for comprehensive profiling of variants.

SureSelect is a proven hybridization-based technology that has been instrumental in advancing NGS. With workflows that provide the fastest hybridization times and different pooling strategies, highly sensitive and accurate variant calling performance is achieved with either large exome captures or highly targeted panels.

HaloPlex is a library prep-free next generation PCR technology that enables streamlined workflows for target enrichment. This technology leverages the high coverage and specificity of PCR while providing amplicon redundancy to ensure target coverage. This FFPE-compatible technology has been used in the discovery of variants involved in the biological mechanisms of cancer.

ClearSeq Disease Research panels are catalog designs developed in collaboration with leading medical genetics experts. These constitutional panels provide deep target coverage for confident variant identification.

OneSeq is an industry first for copy number and mutation detection in one streamlined assay. Powered by SureSelect, combined genome-wide backbone probes along with probes targeting genes enables CNV and LOH detection, in addition to identification of SNPs and InDels.

Publications

Researchers have shown that target enrichment methods such as whole exome sequencing is a very effective approach for discovering the causal mutation for inherited diseases. This method enables thousands of regions to be analyzed simultaneously facilitating detection of genomic variants and has been successfully used in the identification of the causal genes for over 50 Mendelian disorders.

See how **Agilent's NGS Target Enrichment** has revolutionized constitutional disease research

Rare Mendelian Disorders:

1. Martignetti JA *et al*. Mutations in PDGFRB Cause Autosomal Dominant Infantile Myofibromatosis. Am J. Hum. Genet 2013

2. Shearer AE. Comprehensive genetic testing for hereditary hearing loss using massively parallel sequencing. PNAS 2011

3. Nectoux J. Detection of TRIM32 deletions in LGMD patients analyzed by a combined CGH array and massively parallel sequencing. Eur J Hum Genet 2014

4. Rousseau-Nepton I. A founder AGL mutation in glycogen storage disease type III in Inuit identified through whole exome sequencing CMAJ 2015

Complex Disorders:

1. Griesi-Oliveira K *et al*. Modeling non-syndromic autism and the impact of TRPC6 disruption in human neurons Mol Psych 2014

2. Guipponi M *et al*. Exome Seq in 53 sporadic cases of schizophrenia identifies 18 putative candidate genes. PLOS One 2014

3. Poultney CS *et al*. Identification of small exonic CNV from WES data and application to autism spectrum disorder. Am J Med Genet 2013

4. Perez-Serra A *et al*. A novel mutation in lamin a/c causing familial dilated cardiomyopathy associated with sudden cardiac death. J Card Fail 2015

Mitochondrial Disorders:

1. Gai X Mutations in FBXL4 encoding a mitochondrial protein cause early onset mitochondrial encephalomyopathy. Am J Hum Genet 2013

2. Calvo SE.Mol Dx of Infantile Mito Disease with Targeted NGS_Sci Transl Med 2012

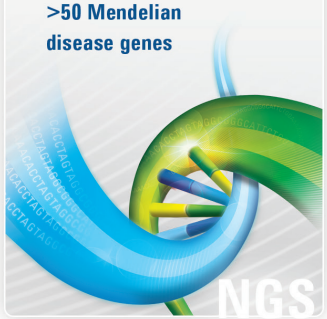
Unrivaled Content Tailored for Clinical Research

Efforts to provide streamlined solutions for constitutional research have led to the introduction of three highly optimized designs that enable compatibility with both high-output and desktop sequencers that pave the way to identification of disease-associated variants: **SureSelect Clinical Research Exome**, **OneSeq Constitutional Research Panel**, **SureSelect Focused Exome**, and **ClearSeq Inherited Disease**.

These **expert-optimized designs** enable highly sensitive and accurate variant calling by providing **deep target coverage with minimal sequencing enabling trio analysis**.

Did You Know?

Agilent NGS solutions have **enabled discoveries detailed in >650 peer-reviewed publications** and has led to **identification of >50 Mendelian disease genes**



High-output → **Desktop**

	Basic/Translational Research				Clinical Research
	SureSelect Human All Exon V6	**SureSelect Clinical Research Exome**	**OneSeq Constitutional Research Panel**	**SureSelect Focused Exome**	**ClearSeq Inherited Disease**
Capture Size and # Genes	**60Mb whole exome**	**54Mb whole exome**	**28Mb Genome-wide backbone with Focused Exome**	**16Mb ~5700 genes**	**10.5Mb ~2800 genes**
Key Features	Best uniformity, best exome-wide breadth and depth of coverage	Increased depth in disease-associated regions	Combined CNV, LOH and mutation detection in one capture	Desktop exome ONLY disease-associated targets	ONLY targets genes known to cause inherited disorders
Recommended for	High-output			Desktop (recommended) Or High-output	Desktop

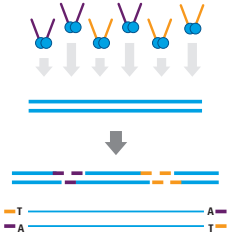
Fastest Workflows, Enriched Libraries in 1 Day

Complement the best content with the accelerated enrichment workflow of **SureSelect^{QXT}** which enables the revolutionary 90-minute hybridization, for faster sample to answers

1 Ordering a Catalog Bait Library or Creating a Custom Panel

Order an NGS catalog panel or easily design a custom panel in minutes using Agilent's SureDesign web application

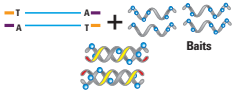
2 Preparation of DNA Libraries



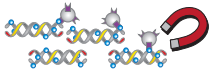
Genomic DNA is enzymatically fragmented and tagged with the adaptors

Adaptor-tagged fragments are amplified to generate the pre-capture libraries

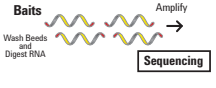
3 Hybridization and Capture



a. DNA library is allowed to hybridize with biotinylated SureSelect RNA baits (90 min for QXT)



b. DNA-RNA hybrids are pulled down using streptavidin-coated magnetic beads



c. Stringent washes are applied to eliminate non-specific targets

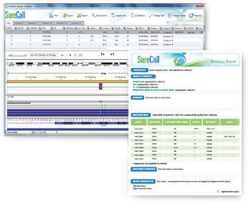
4 Amplification of Enriched Libraries

Indexes are added to the enriched library using on-bead PCR

5 QC Final Library

Quantify and QC prepared libraries using a 2200 TapeStation or 2100 Bioanalyzer System

6 Sequencing and Data Analysis



Sequence libraries, analyze and obtain report of mutations using SureCall data analysis software

NGS Constitutional Disease Research Resource Center

Revolutionizing Clinical Research

Providing streamlined solutions for identification of disease-associated variants.

For more information:

www.agilent.com/genomics/NGSConstitutional

To request more information or get a demo, call your Agilent Sales Representative.

CALL OR LEARN MORE AT:

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