

NGS Cancer Research Solutions

Target Enrichment Systems



Agilent Technologies

AGILENT NGS: MAKING AN IMPACT MEANS CHANGING LIVES

Agilent offers a full range of catalog and custom target enrichment solutions that enable a streamlined workflow tailored to meet specific needs such as 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 exome captures or highly targeted panels.

HaloPlex^{HS} is a high-sensitivity, next generation PCR method that incorporates unique molecular barcodes in the DNA library. This FFPE-compatible technology allows for the identification of duplicate reads, significantly improving base calling accuracy at low allelic frequencies in heterogenous cancer samples.

ClearSeq Cancer research panels are catalog designs focused on targeted gene sets for comprehensive detection of somatic variants in solid tumors and hematological cancers. Developed in collaboration with leading cancer research experts, these panels enable clinical researchers to confidently identify mutations, indels and gene fusions from FFPE, blood and bone marrow samples.



HIGH SENSITIVITY FOR DETECTION OF RARE VARIANTS

Highly targeted panels enable deeper coverage for accurate and comprehensive identification of somatic variants in solid tumors and hematological cancers. Combined with low-input, FFPE-compatible workflows that enable high-sensitivity detection, Agilent provides a rapid and complete sample-to-data solution.

Catalog Designs Optimized for Cancer Research

Enrichment Technology	Product Name	Features
SureSelect	SureSelect Human All Exon V6+COSMIC	Comprehensive exome-wide analysis including COSMIC targets
	SureSelect Human MethylSeq	Analysis of differentially methylated regions in the genome that impact gene regulation
	ClearSeq Comprehensive Cancer	Enables analysis of 151 key genes associated in a wide range of cancers
	ClearSeq DNA and RNA Kinome	Analysis of kinome including UTRs
HaloPlex ^{HS}	ClearSeq Cancer ^{HS}	Identify somatic variants in 47 genes containing COSMIC hotspots
HaloPlex	ClearSeq AML	Deep coverage of 20 genes frequently mutated in acute myeloid leukemia

Did You Know?

SureSelect

The standard in Target Enrichment (>500 kb)

- Large captures
- Translocations
- RNA captures

HaloPlex^{HS}

High sensitivity for Rare Variant Detection

- Small captures (≤500 kb)
- Identify variants with <1% allele frequency

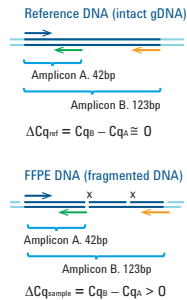
ACCELERATED WORKFLOWS, BETTER ANSWERS

1 Ordering a Catalog Bait Library or Creating a Custom Panel



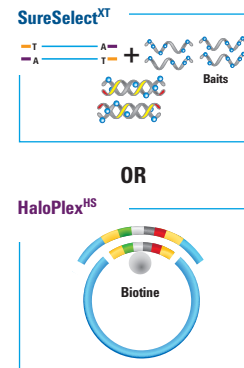
Order an NGS catalog panel or easily design a custom panel in minutes using Agilent's SureDesign web application.

2 Quantify and Qualify DNA Input



1. Sample quantitation based upon DNA of known concentrations.
2. DNA quality score (ddCq) is determined based on relative amplification of a small 42 bp vs a long 123 bp fragment.
3. 200 ng of amplifiable DNA is taken into the SureSelect or HaloPlex workflow. Optimizations based upon quality are provided.

3 Hybridization and Capture



DNA library is hybridized with biotinylated **SureSelect RNA baits** or **HaloPlex^{HS} probes**. Targets are pulled down by streptavidin beads and washed 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 quality control libraries using a 4200 TapeStation or 2100 Bioanalyzer System.

6 Sequencing and Data Analysis



Sequence libraries. Analyze and obtain report of mutations using SureCall data analysis software.

PUBLICATIONS

Targeted resequencing has proven to be an effective approach for identifying driver mutations in cancer, given that deep sequencing is often required to achieve coverage of low frequency variants.

See how **Agilent's NGS Target Enrichment** has advanced cancer research.

Solid Tumors:

1. Walsh T, *et al.* Detection of inherited mutations for breast and ovarian cancer using genomic capture and massively parallel sequencing. *PNAS* (2010) 107:12629-3.
2. Ramos P, *et al.* Small cell carcinoma of the ovary, hypercalcemic type, displays frequent inactivating germline and somatic mutations in SMARCA4. *Nat. Gen.* (2014) 46:427-9.
3. Van Allen EM, *et al.* Whole-exome sequencing and clinical interpretation of formalin-fixed, paraffin-embedded tumor samples to guide precision cancer medicine. *Nat. Med.* (2014) 20:682-8.
4. Robles-Espinoza CD, *et al.* POT1 loss-of-function variants predispose to familial melanoma. *Nat Gen.* (2014) 46:478-81.
5. Aihara K, *et al.* H3F3A K27M mutations in thalamic gliomas from young adult patients. *Neuro Oncol.* (2014) 16:140-6.
6. Koopmans AE, *et al.* Patient survival in uveal melanoma is not affected by oncogenic mutations in GNAQ and GNA11. *British J. Cancer* (2013) 109:493-6.
7. Suzuki A, *et al.* Aberrant transcriptional regulations in cancers: genome, transcriptome and epigenome analysis of lung adenocarcinoma cell lines. *Nucleic Acids Res.* (2014) 42:13557-72.
8. Sugita S, *et al.* A novel CIC-FOXO4 gene fusion in undifferentiated small round cell sarcoma: a genetically distinct variant of Ewing-like sarcoma. *Am J Surg Pathol.* (2014) 38:1571-6.
9. Tuononen K, *et al.* Targeted resequencing reveals ALK fusions in non-small cell lung carcinomas detected by FISH, immunohistochemistry, and real-time RT-PCR: A comparison of four methods. *BioMed Res. Int.* (2013) 757490 epub doi: 10.1155/2013/757490.
10. Oike T, *et al.* A synthetic lethality-based strategy to treat cancers harboring a genetic deficiency in the chromatin remodeling factor BRG1. *Cancer Res.* (2013) 3:5508-18.

Hematological Cancers:

1. Mansouri L, *et al.* Feasibility of targeted next-generation sequencing of the TP53 and ATM genes in chronic lymphocytic leukemia. *Leukemia* (2014) 28:694-6.
2. Menezes J, *et al.* CSF3R T618I co-occurs with mutations of splicing and epigenetic genes and with a new PIM3 truncated fusion gene in chronic neutrophilic leukemia. *Blood Cancer J.* (2013) e158. doi: 10.1038/bcj.2013.55.
3. Berglund EC, *et al.* Accurate detection of subclonal single nucleotide variants in whole genome amplified and pooled cancer samples using HaloPlex target enrichment. *BMC Genomics* (2013) 14:856.
4. Schulz E, *et al.* Germline mutations in the DNA damage response genes BRCA1, BRCA2, BARD1 and TP53 in patients with therapy related myeloid neoplasms. *J Med. Genet.* (2012) 49:422-8.
5. Hájková H, *et al.* CBFB-MYH11 hypomethylation signature and PBX3 differential methylation revealed by targeted bisulfite sequencing in patients with acute myeloid leukemia. *J Hematol Oncol.* (2014) 7:66.
6. Miura F, *et al.* Highly sensitive targeted methylome sequencing by post-bisulfite adaptor tagging. *DNA Res.* (2014) 22:13-8.
7. Halvardson J, *et al.* Exome RNA sequencing reveals rare and novel alternative transcripts *Nucleic Acids Res.* (2013) 41:e6. doi: 10.1093/nar/gks816.
8. Ueno T, *et al.* High-throughput resequencing of target-captured cDNA in cancer cells. *Cancer Sci.* (2012) 103:131-5.
9. Levin JZ, *et al.* Targeted next-generation sequencing of a cancer transcriptome enhances detection of sequence variants and novel fusion transcripts. *Genome Biol.* (2009) 10:R115.
10. Vogelzang A, *et al.* IL-21 contributes to fatal inflammatory disease in the absence of Foxp3+ T regulatory cells. *J Immunol.* (2014) 192:1404-14.

NGS CANCER RESEARCH RESOURCE CENTER

Enabling accurate and comprehensive identification of somatic variants in solid tumors and hematological cancers.

For more information:

www.agilent.com/genomics/NGSCancer



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PR7000-0289

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Printed in USA, October 18, 2016

5991-5988EN

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