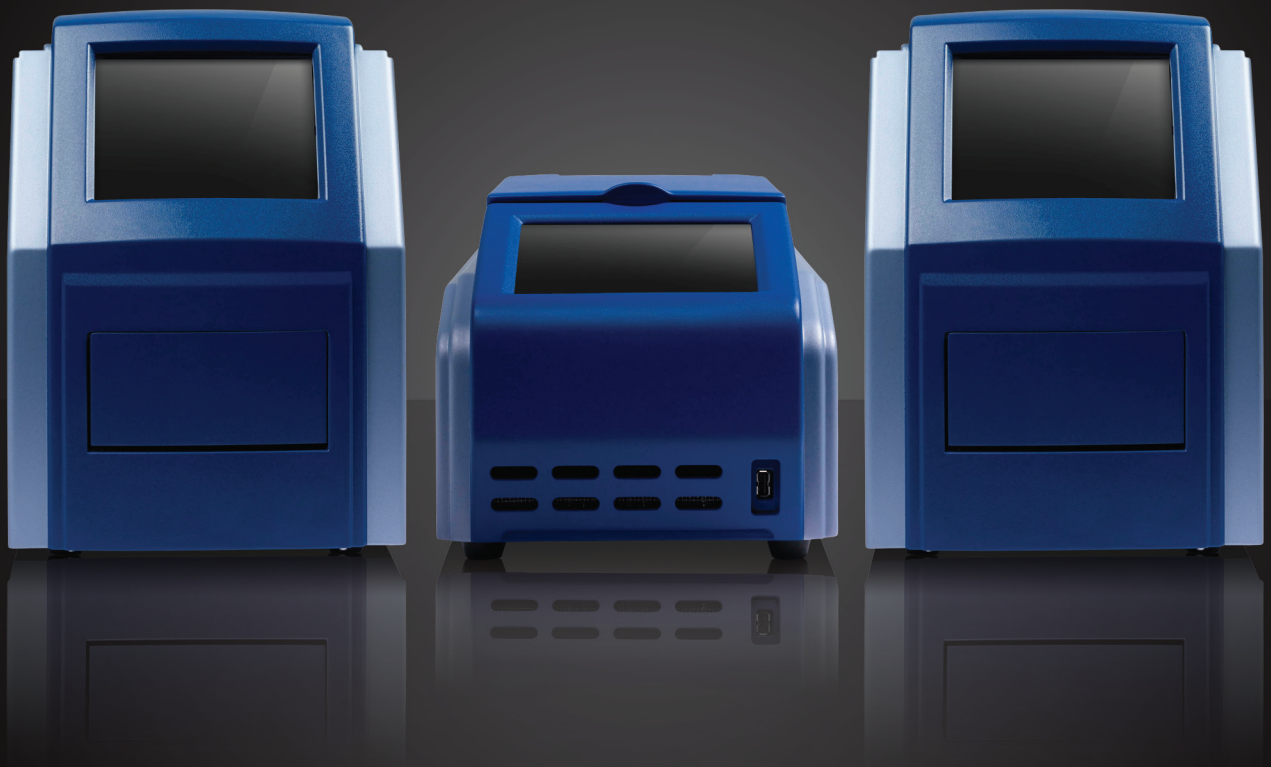
FLUIDIGM

SEQUENCING

From Sample to Sequence-Ready



ACCESS ARRAY™ SYSTEM

HIGH-QUALITY LIBRARIES, NOT ONCE, BUT EVERY TIME

- The highest-quality amplicons—more sensitive, accurate, and specific
- Full support for all major next-generation sequencing platforms
- Shortest hands-on time at the lowest running cost

The Promise of Next-Generation Sequencing

Next-Generation Sequencing (NGS) technologies have transformed life science research, enabling many new sequencing-based applications. One of the most promising is targeted sequencing, to identify variations relevant to cancer, disease research, and population genetics. Using NGS as the foundation for a targeted sequencing approach promises to provide quantitative insight into mutations, in context, in a single run, at greater throughput, and at lower cost than previously seen. The Access Array System, combined with next-generation sequencing, is a powerful approach for comprehensive genotyping, validation, and screening analyses, including SNP identification, sequence variation and mutation detection, DNA methylation mapping, and exon sequencing—across hundreds of samples.

Library preparation is the foundation for a successful targeted sequencing run. However, traditional methods create bottlenecks and introduce risk to quality and reproducibility through the high number of steps and touch points in the protocols. The Access Array System, through its system of controllers and integrated fluidic circuits (IFCs), encapsulates library preparation to provide unparalleled quality amplicons. The Access Array System takes DNA from sample to sequence-ready.

The Access Array System: from Sample to Sequence, Ready for Next-Generation Sequencing

Regardless of your choice of sequencer for targeted sequencing, you must always first create a library, or a molecular construct that has the adaptors necessary for clonal amplification and sequencing appended to the ends of your targeted region. The specificity and sensitivity of PCR makes it ideal for a variety of amplicon library creation strategies. The Access Array System is the only high-throughput target enrichment system designed to work with all major next-generation sequencing instruments. You can now enrich hundreds of unique targets (such as exons) from a large number of samples all at once. The system combines the cost and throughput benefits of microfluidics with the proven performance and flexibility of PCR while reducing hands-on time to produce superb uniformity in the library construct.

The Access Array™ System is comprised of a thermal cycler, a pre-PCR IFC Controller AX for loading samples, and a post-PCR IFC Controller AX for harvesting amplified products.

Scalable and Flexible

The Access Array System is highly scalable because of its modular design and simple workflow. A library prepared on a single Access Array IFC is an ideal fit for complete experiments on a variety of benchtop sequencers. Multiple IFCs can may be tiled to generate libraries that match the throughput of the largest next-generation sequencers.

LITERARY PREPARATION	CLONAL AMPLIFICATION	SEQUENCING	ANALYSIS

The Access Array System is the foundation of successful targeted sequencing.

Make the Promise of Next-Generation Targeted Resequencing a Reality

Access Array Target-Specific Primers

Access Array Target-Specific Primers provide fast, simple, and inexpensive preparation of sequencing-ready libraries. Take full advantage of your Access Array System with minimal experiment setup time while producing robust results.

Access Array IFC

- Study only your regions of interest with custom-designed primer sets.
- Bypass traditional library prep with amplicon tagging, saving time and cost.
- Boost throughput and scalability: multiplex up to 480 amplicons per sample.

The Access Array IFC enables researchers to perform nanoliter-volume, high-throughput PCR. Each IFC accommodates up to 23,040 amplicons in a single run.

Access Array Target-Specific Primers are customized to meet your requirements. When used with the Access Array System, the primers allow for preparation of up to 480 unique amplicons across 48 samples. Simply provide us with your regions of interest for the human genome; we will design primer sets to amplify (and tag) PCR products for sequencing.

DATA QUALITY

Excellent sample and amplicon uniformity produce high-quality data and enable powerful data analysis.

HIGH THROUGHPUT

Simultaneously enrich targets of interest from 48 samples at a time. When used with the Access Array Barcode Library, each library is uniquely tagged, so up to 384 samples can be pooled and sequenced in a single multiplex sequencing run with no additional library preparation.

EASE OF USE

In three steps with 20 minutes of hands-on time, produce 48 sequence-ready libraries.

OPEN PLATFORM

The Access Array IFC is compatible with most PCR-based enrichment technology, including amplicon tagging, long-range PCR, and multiplex PCR. Libraries can be tagged to be compatible with all major next-generation sequencing platforms, including the Roche® 454; Illumina® GAIIx™, HiSeq®, and MiSeq™; and Ion Torrent™ PGM™ systems.

Easy Workflow

An entire target enrichment experiment from DNA to a finished amplicon library can be carried out in three simple steps, and completed in four hours with only 20 minutes of hands-on time.

Targeted Sequencing, Simplified

The Access Array System builds the highest-quality amplicon libraries in the fastest hands-on time at lowest running cost for all major NGS platforms. Your amplicon libraries will have:

- **Homogeneity**—85% uniformity of coverage
- **Accuracy**—90% mapped to genome*
- **Specificity**—95% mapped to target
- **Minimal input**—50 ng input DNA (10ng with pre-amplification)
- **Reduced errors**—streamlined workflow with just 20 minutes of hands-on time
- **Support**—compatible with Illumina GAIIx, HiSeq, and MiSeq sequencers; Ion Torrent PGM; and Roche 454

Simple Process

Complete Experiments in Three Easy Steps

1 **LOAD**

In the pre-PCR IFC Controller AX, samples and primers are automatically combined into 2,304 unique PCR reactions.

2 **AMPLIFY**

The IFC is placed in the FC1™ cycler for target amplification.

3 **HARVEST**

After PCR, products from each sample are pooled on the IFC in the post-PCR IFC Controller AX and pumped out for collection.

* Illumina platforms only. Ion Torrent PGM achieves a mapping to genome score of >75% related to emPCR. However, uniformity and mapped-to-target scores remain in line with other supported platforms.

AMPLIFICATION, TAGGING, BARCODING

In the amplicon tagging protocol, primers attach sample-specific barcode sequences and sequencer-specific tags to each PCR product. Primers can be multiplexed to build libraries of 480 amplicons per sample, or up to 23,040 per run. Barcode sequences allow up to 384 samples to be pooled and sequenced in one multiplex sequencing reaction.

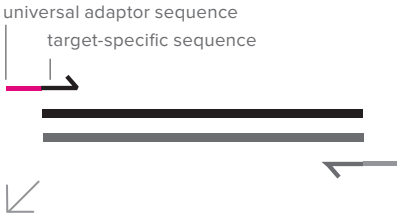
Four-Primer Amplicon Tagging

While the Access Array System can be used for nearly any PCR-based enrichment strategy, four-primer amplicon tagging with Fluidigm protocols and reagents is ideal for creating amplicon libraries for any next-generation sequencing platform. In four-primer amplicon tagging, the inclusion of a short consensus sequence (CS) tag onto the 5' end of the target-specific primer and the 3' end of the sequencing adaptor allows you to design and validate any target-specific primers, regardless of the sequencer type or level of sample multiplexing required. The barcode oligos with CS linkers are universal reagents in the four-primer amplicon tagging protocol and can be used with any target-specific primer sequences, greatly reducing the number of unique oligos required to conduct multiple-target resequencing experiments.

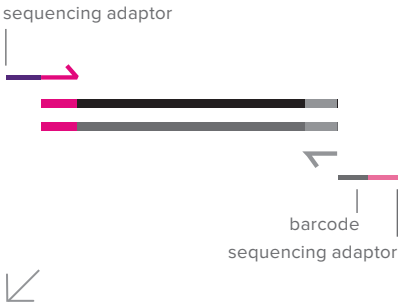
Targeted Sequencing Simplified

Complete Experiments in Three Easy Steps

1 Hybridization of sequence-specific primers to appropriate region of genomic DNA. Primers contain universal tag sequences to allow binding of barcode primers.



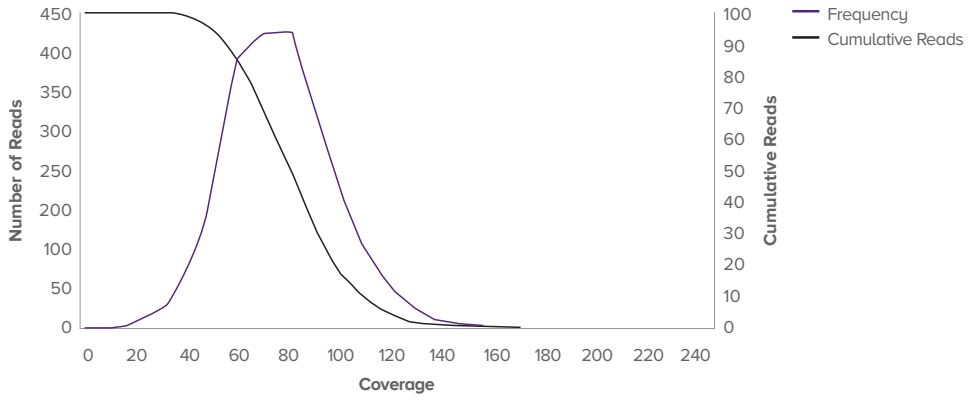
2 Hybridization of barcode primers, which also contain a capture sequence appropriate for sequencer chemistry.



3 Final amplicon containing barcode sequence to identify parent DNA sample, tagged for capture and entry into emPCR.

Even Representation of Enriched Sequences

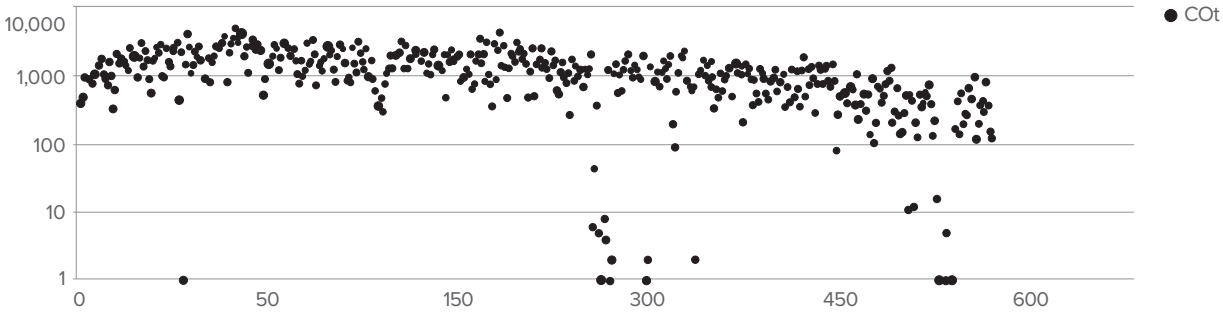
The Access Array System provides high-quality data with uniform sequence representation across multiple targets and samples; these two features maximize your sequence's utility. The figure below shows the representation of 2,304 amplicons generated from 48 genomic DNA samples and 48 different sequence-specific primer sets. More than 95% of the amplicons demonstrate coverage within two-fold of the average. More consistent amplicon generation during library preparation means more even distribution of sequencing reads across all samples and less time and money spent on sequencing.



Uniform sequence representation of 48 unique amplicons from 48 genomic DNA samples

Multiplex PCR for Increased Sequence Coverage

The amount of sequence enriched per sample is highly scalable with multiplex PCR protocols. Each sample can be enriched using as few as 48 primer pairs in singleplex mode, up to as many as 480 primer pairs in multiplex mode. The unique protocol and specific IFCs developed for the Access Array System maintain data quality in terms of representation or uniformity when used in a 10-plex format.



Coverage achieved for 480 cancer-specific exons in a 48 x 10-plex amplicon pool from a single 48.48 Access Array IFC

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HIGH-QUALITY NGS RESULTS, NOT ONCE, BUT EVERY TIME

The era of next-generation sequencing arrived with a great deal of promise, and much of that promise is based on dependable, accurate, and specific sample preparation. There are other methods for sample preparation, but only one considered the most straightforward and least error-prone. Easily move from sample to sequence-ready, not once, but every time with the Access Array System, today.

Find out more at fluidigm.com

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