DATA SHEET

Illumina DNA Prep with Enrichment

Fast, integrated workflow for a wide range of target enrichment applications

- Provides a time-saving solution that is 85% faster than standard Illumina library prep and enrichment
- Enhances library preparation efficiency with integrated protocols for blood and saliva
- Enables advanced study designs in cancer research, genetic disease research, and whole-exome sequencing

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Introduction

The Illumina DNA Prep with Enrichment solution combines versatile, simple, and fast library prep and enrichment functionality for targeted enrichment and exome sequencing applications. It offers extraordinary flexibility for input type and amount (Table 1), and a wide range of supported enrichment sequencing applications encompassing custom panels, fixed panels, and whole-exome sequencing from Illumina or third-party vendors.

Illumina DNA Prep with Enrichment uses innovative bead-based chemistry incorporating a simplified, single hybridization step (Figure 1). With the Illumina DNA Prep with Enrichment workflow, DNA extraction can be processed directly from fresh blood and saliva samples using the Flex Lysis Reagent Kit and Saliva Lysis Protocol, respectively, for additional time savings.

Table 1: Illumina DNA Prep with Enrichment specifications

Parameter	Specification
DNA input type	gDNA, whole blood, saliva, DNA extracted from formalin-fixed, paraffin-embedded (FFPE) tissue
DNA input verified[a]	10–1000 ng
Sample multiplexing	384 unique dual indexes (UDIs)
Pre-enrichment pooling[b]	1-plex or 12-plex verified and supported
Supported sequencing systems	All Illumina systems
Total workflow time[c]	~6.5 hours

a. DNA inputs as low as 10 ng are possible, but will not provide saturation-based DNA normalization.
b. Other enrichment plexities are possible, but have not been verified. Additional optimization may be required and optimal results are not guaranteed.
c. Includes library preparation, enrichment, and library normalization/pooling steps.

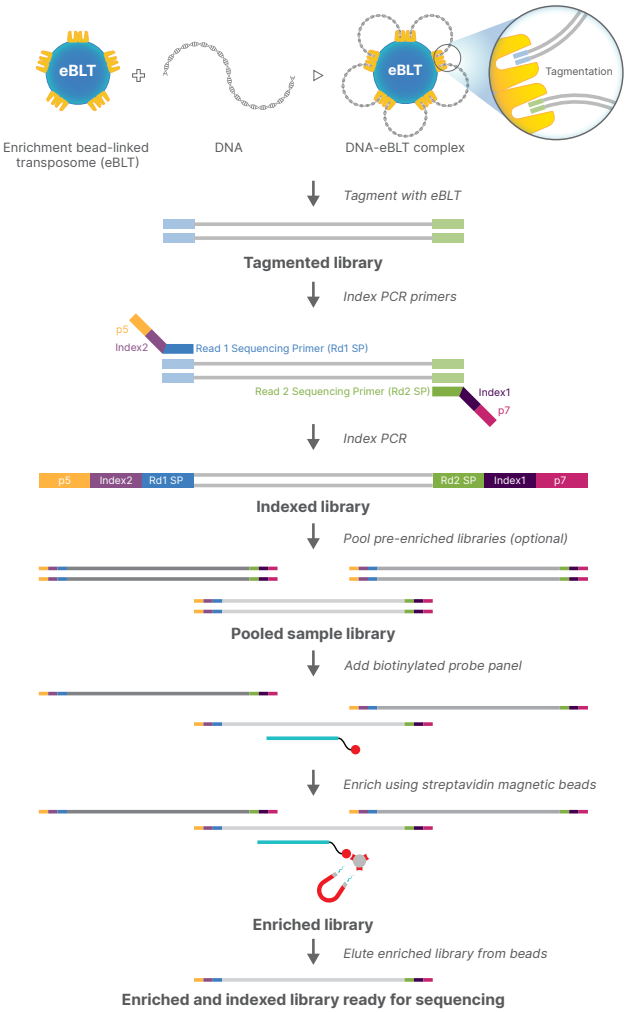

Figure 1: Illumina tagmentation chemistry—A uniform tagmentation reaction mediated by eBLTs followed by a single hybridization reaction enables a fast and flexible workflow.

Fast and flexible library preparation and enrichment workflow

A key component of the Illumina DNA Prep with Enrichment solution is on-bead tagmentation, which uses bead-bound transposomes to mediate a uniform tagmentation reaction. This strategy provides several significant advantages:

- For gDNA inputs ≥ 50 ng, accurate quantitation of the initial DNA sample is not required, as insert fragment size is not affected, saving time and costs associated with kits and reagents
- On-bead tagmentation eliminates the need for separate DNA fragmentation steps, saving time and costs associated with related consumables
- For gDNA inputs of 50–1000 ng, saturation-based DNA normalization eliminates the need for individual library quantitation and normalization steps before enrichment
- Novel 90-minute single hybridization protocol enables enrichment in less than four hours

Fastest Illumina enrichment workflow

The Illumina DNA Prep with Enrichment solution supports liquid-handling systems for library prep automation and produces a workflow with the fewest number of steps and the fastest total workflow time in the Illumina enrichment portfolio (Figure 2, Table 2).

Integrated DNA Input

DNA extraction can be processed directly from whole blood or saliva samples. The optional Flex Lysis Reagent Kit, optimized and validated for using whole blood samples and Illumina DNA Prep with Enrichment, is integrated into the workflow for maximum efficiency. The lysis protocols feature bead-based reagents and require less than 30 minutes of hands-on time.

Optimized performance across Illumina sequencing systems

The robust and straightforward Illumina DNA Prep with Enrichment solution yields reliable results across all Illumina sequencing systems by providing > 90% on-target reads, > 95% uniformity, and a low PCR duplicate rate (Table 3). Illumina DNA Prep with Enrichment is compatible with various Illumina enrichment panels and is optimized for use on low-, mid-, and high-throughput systems (Figure 3, Table 4).

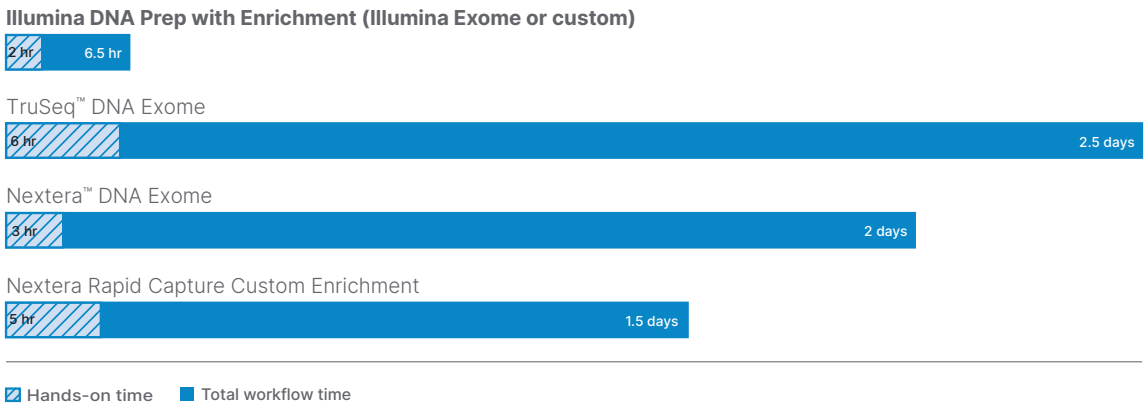

Figure 2: Illumina DNA Prep with Enrichment delivers the fastest Illumina enrichment workflow—Workflow times are based on processing 12 samples at 12-plex enrichment. Times may vary depending on equipment used, number of samples processed, automation procedures, or user experience.

Table 2: Comparison of Illumina enrichment workflows

	Illumina DNA Prep with Enrichment	TruSeq DNA Exome	Nextera DNA Exome	Nextera Rapid Capture Custom Enrichment
Integrated DNA option[a]	√	—	—	—
Flexible, broad DNA input range	√	—	—	—
Library normalization included[b]	√	—	—	—
FFPE compatible	√	√	—	—
DNA input	10–1000 ng	100 ng	50 ng	50 ng
Total library prep and enrichment time[c]	~6.5 hr	2.5 days	2 days	1.5 days
Insert size[d]	150–220 bp	150 bp	150–220 bp	230 bp
Sample index sets	384 unique dual indexes	24 single indexes, 96 dual indexes	24 single indexes, 96 dual indexes	24 single indexes, 96 dual indexes

a. Integrated lysis protocols available for blood and saliva.
b. Library normalization occurs with ≥ 50 ng gDNA input.
c. Total library prep and enrichment time includes library preparation, library normalization/pooling, and enrichment.
d. Degraded FFPE DNA may result in smaller insert sizes.

Table 3: Performance comparison across Illumina enrichment workflows[a]

Parameter[b]	Illumina DNA Prep with Enrichment	Illumina DNA Prep with Enrichment	Illumina DNA Prep with Enrichment	TruSeq DNA Exome	Nextera DNA Exome
Panel	Illumina Exome Panel[c]	Exome Panel X	Exome Panel Y	Illumina Exome Panel	Illumina Exome Panel
Panel size	45 Mb	39 Mb	33 Mb	45 Mb	45 Mb
Probe size	80 bp	120 bp	120 bp	80 bp	80 bp
Padded read enrichment (on-target)[d]	85%	91%	91%	85%	75%
Fragment length median	~200 bp	~200 bp	~200 bp	~150 bp	~200 bp
Coverage at 20×	93%	96%	97%	90%	85%
Uniformity of coverage[d]	95%	97%	98%	85%	85%
Read depth per sample[e]	30M CPF	25M CPF	20M CPF	40M CPF	40M CPF
SNV precision	99%	99%	99%	99%	99%
SNV recall	94%	94%	95%	89%	91%

a. Data represents example comparison data. Actual performance specifications may vary depending on read depth and sample type.
b. The analysis was run on 48 samples (all NA12878 Coriell samples) per condition. Data analysis was performed using the Enrichment BaseSpace™ App.
c. Illumina DNA Prep with Exome 2.5 Enrichment is the recommended solution for human exome sequencing.
d. See the BaseSpace™ App User Guide[2] for additional details.
e. CPF, clusters passing filter.

Figure 3: Optimized performance across Illumina sequencing systems—The Illumina DNA Prep with Enrichment solution is compatible with all Illumina sequencing systems, including the high-performance systems shown here. Low-throughput systems including the iSeq™ 100, MiniSeq™, and MiSeq™ Systems are also compatible with Illumina DNA Prep with Enrichment.

Table 4: Sample throughput per flow cell with Illumina DNA Prep with Enrichment[a]

	iSeq 100 System	MiniSeq System		MiSeq System			NextSeq 550 System	
		Mid	High	v2	v2 Nano/Micro	v3	Mid	High
Fixed panels								
TruSight™ One	NR	NR	2	1	0/0	3	12	36
TruSight One Expanded	NR	NR	1	0	0/0	1	7	24
TruSight Cancer	4	8	24	12	1/4	24	96	384
TruSight Hereditary Cancer	4	8	24	12	1/4	24	96	384
Custom panels								
2000 probes	8	16	50	30	2/8	50	260	384
5000 probes	2	4	12	8	1/2	12	65	200
10,000 probes	1	2	6	4	0/1	6	33	100

	NextSeq 550 System		NextSeq 2000 System		NovaSeq 6000 System				NovaSeq X Series		
	Mid	High	P2	P3	SP	S1	S2	S4	1.5B	10B	25B
Exome panel[b]	~4	~12	~10	~30	~20	~41	~104	~250	~41	~250	~750[c]

a. Mid, mid output; High, high output; NR, not recommended.
b. Exomes assume ~8 Gb per sample to achieve 100× coverage.
c. 384 unique dual indexes are available.

Accurate data

Illumina DNA Prep with Enrichment produces highly uniform and consistent insert sizes across a wide DNA input range, delivering uniform and consistent library yields.[1] It also provides high coverage uniformity and padded read enrichment for custom, fixed, and exome panels (Figure 4). Illumina DNA Prep with Enrichment enables accurate single nucleotide variant (SNV) (Figure 5, Table 3) and insertion/deletion (indel) recall and precision, as compared to other Illumina enrichment solutions.

DNA enrichment for a broad range of applications

By combining exceptional enrichment performance and the proven accuracy of Illumina sequencing by synthesis (SBS) chemistry, the Illumina DNA Prep with Enrichment solution supports both fixed and custom panels of varying sizes, including those designed for whole-exome sequencing, for advanced study designs in a variety of areas (Figure 6). Furthermore, Illumina DNA Prep with Enrichment is compatible with Illumina and third-party enrichment probes/panels, enabling content portability for increased flexibility.

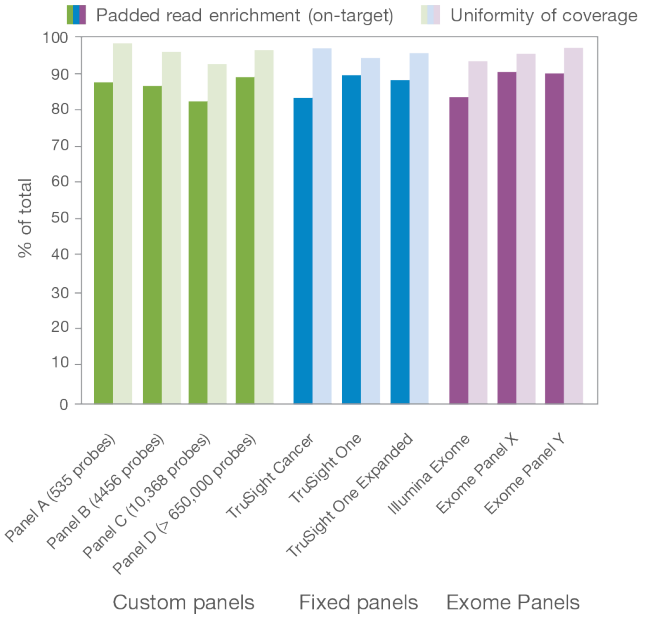

Figure 4: High coverage uniformity and padded read enrichment—Illumina DNA Prep with Enrichment provides high coverage uniformity and on-target padded read enrichment for custom, fixed, and exome panels.

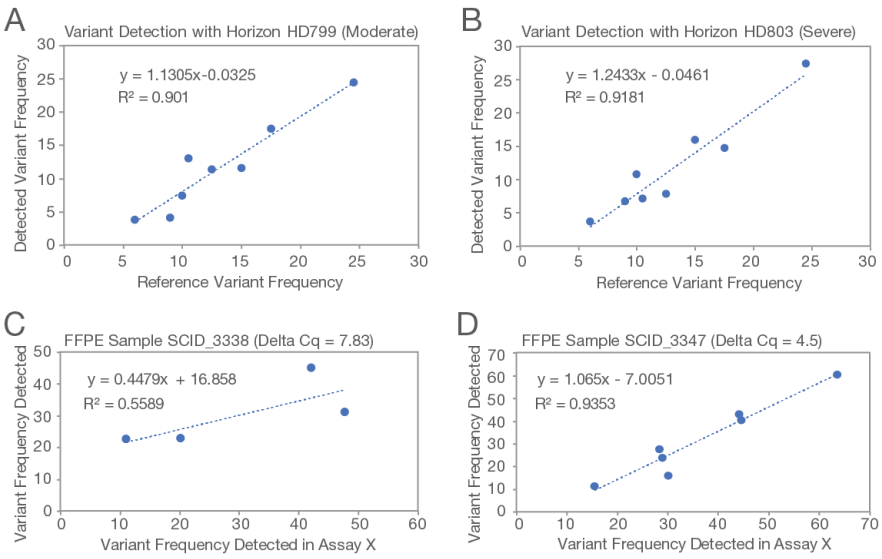

Figure 5: Accurate variant calling—Illumina DNA Prep with Enrichment provides low abundance somatic variant calling for (A, B) cell line FFPE control human reference DNA samples and (C, D) real-world FFPE samples with observed variant frequency showing significant correlation with frequencies from an orthologous sequencing assay.

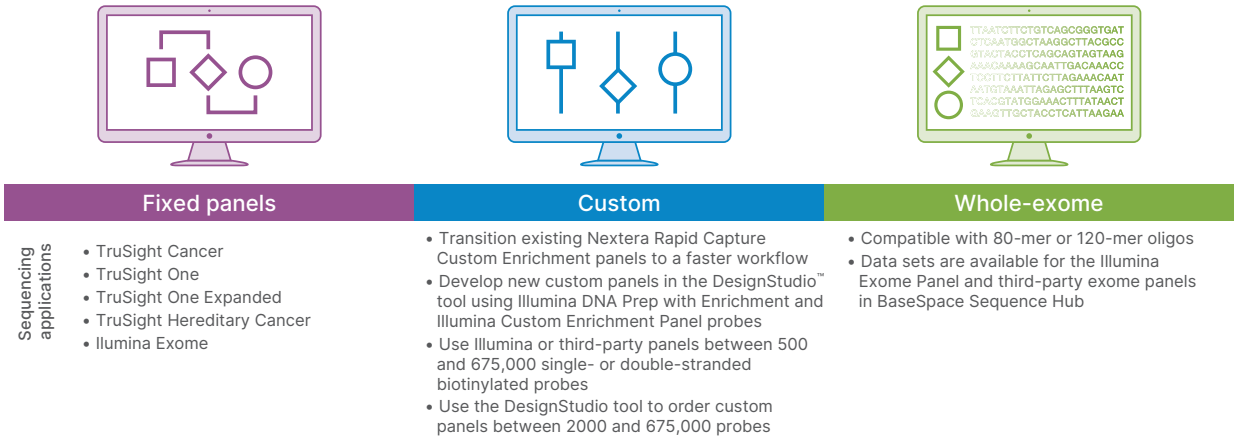

Figure 6: Broad range of applications with Illumina DNA Prep with Enrichment—Illumina DNA Prep with Enrichment supports a broad range of applications, including custom panels, fixed panels, and exome panels.

Summary

Illumina DNA Prep with Enrichment features the fastest workflow in the Illumina enrichment portfolio. The user-friendly, automation-compatible solution supports users of all experience levels and provides a common workflow for a variety of experimental designs, including fixed panels, custom panels, and whole-exome sequencing. On-bead tagmentation enables use of a wide range of DNA input amounts and various sample types. Illumina DNA Prep with Enrichment is compatible with Illumina and third-party enrichment probes/panels, enabling content portability. The innovative Illumina DNA Prep with Enrichment solution combined with the power of Illumina SBS chemistry provides an optimal targeted enrichment and exome sequencing experience.

Learn More

Illumina DNA Prep with Enrichment

On-bead tagmentation

References

1. Illumina. Illumina DNA Prep Data Sheet. illumina.com/content/dam/illumina/gcs/assembled-assets/marketing-literature/illumina-dna-prep-data-sheet-m-gl-10373/illumina-dna-prep-data-sheet-m-gl-10373.pdf. Updated 2022. Accessed August 17, 2023.
2. Illumina. BWA Enrichment v2.1 BaseSpace App Guide. support.illumina.com/content/dam/illumina-support/documents/documentation/software_documentation/basespace/basespace-bwa-enrichment-v2-1-app-guide-15050958-01.pdf. Updated 2016. Accessed September 22, 2023.

Ordering information

Product	Catalog no.
Illumina DNA Prep with Enrichment, (S) Tagmentation (96 samples)	20025524
Illumina DNA Prep with Enrichment, (S) Tagmentation (16 samples)	20025523
Flex Lysis Reagent Kit	20018706
Illumina DNA/RNA UD Indexes Set A, Tagmentation (96 indexes, 96 samples)	20091654
Illumina DNA/RNA UD Indexes Set B, Tagmentation (96 indexes, 96 samples)	20091656
Illumina DNA/RNA UD Indexes Set C, Tagmentation (96 indexes, 96 samples)	20091658
Illumina DNA/RNA UD Indexes Set D, Tagmentation (96 indexes, 96 samples)	20091660
TruSight Cancer (8 enrichment reactions)	FC-121-0202
TruSight One (6 enrichment reactions)	20029227
TruSight One Expanded (6 enrichment reactions)	20029226
TruSeq Hereditary Cancer (8 enrichment reactions)	20029551
Illumina Custom Enrichment Panel	20025371

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