

## Product Profile

# QIAseq<sup>®</sup> Multimodal Panels

For simultaneous DNA and RNA profiling

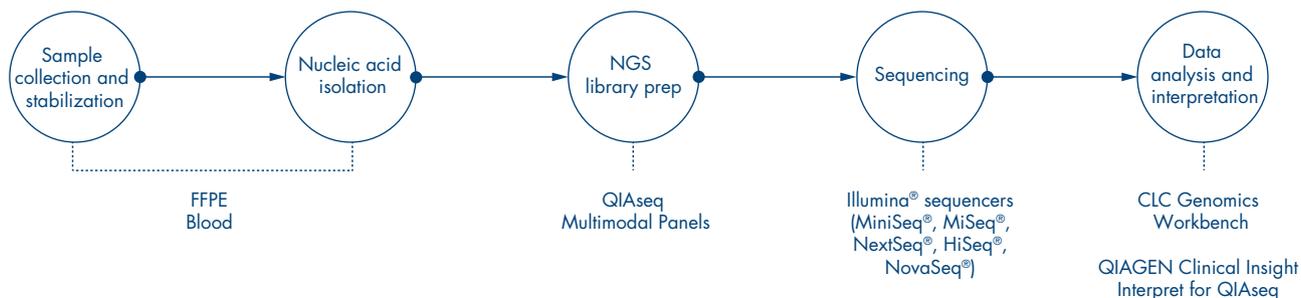
The QIAseq Multimodal Panels offer:

- A single-day workflow to go from total nucleic acids to sequencing-ready libraries
- Error correction with unique molecular indices (UMIs) to enhance NGS panel sensitivity
- A single primer extension (SPE) approach without a predefined amplicon size constraint
- Unique dual indices (UDIs) to reduce sample index hopping
- A Sample to Insight<sup>®</sup> solution for consolidated targeted DNA and RNA sequencing

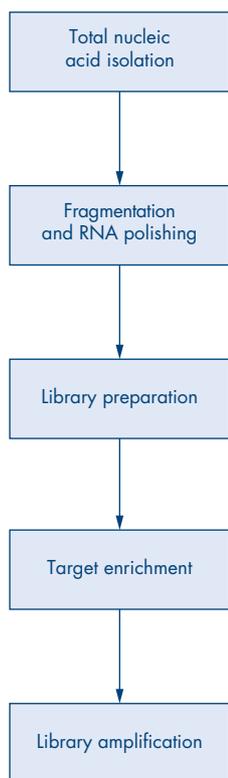
Recent advances in NGS chemistries, platforms and bioinformatics pipelines have empowered users to efficiently interrogate DNA and RNA modifications in biological samples. Current approaches, however, require the use of two separate library prep workflows – one each for DNA and RNA. Further limitations of current approaches include: (1) higher sample input requirements to generate adequate DNA and RNA, (2) inefficient use of resources, (3) long turnaround times and (4) the added complexity of deriving integrated insights from different technical approaches, each with its own innate bias.

The QIAseq Multimodal Panels overcome these limitations by consolidating targeted DNA and RNA enrichment and analyses. Unlike current approaches, QIAseq Multimodal Panels do not require two separate workflows for DNA and RNA analyses, saving time and limited samples. With QIAseq Multimodal Panels, you can use total nucleic acids (DNA and RNA) as starting input to prepare UDI-containing, Illumina<sup>®</sup>-compatible targeted DNA and RNA libraries, using a single-day, consolidated workflow.

This Sample to Insight workflow (Figure 1) can be used to interrogate different types of biomarkers from total nucleic acids (Table 1). Dedicated sample isolation protocols have been developed specifically for the QIAseq Multimodal Panels to enable isolation of total nucleic acids from multiple sample types.



**Figure 1. Extract more information, while reducing sample, time and cost with a simple, one-day workflow.** This flexible solution enables the construction of Illumina-compatible libraries from as little as 10 ng total nucleic acid isolated from a wide range of samples. The data analysis pipelines in CLC Genomics Workbench translate raw sequence data in FASTQ format to DNA and RNA variant files (VCFs), which can be further interpreted for biological significance through QCI® Interpret for QIAseq.



QIAseq Multimodal Panels offer a streamlined, consolidated one-day workflow

The QIAseq Multimodal workflow can be used to prepare sequencing-ready libraries in a day (Figure 2). Representative libraries generated using the QIAseq Multimodal Panels are shown in Figure 3. The library insert size is approximately 150 bp, making the QIAseq Multimodal Panels highly compatible with low-quality samples such as FFPE samples.

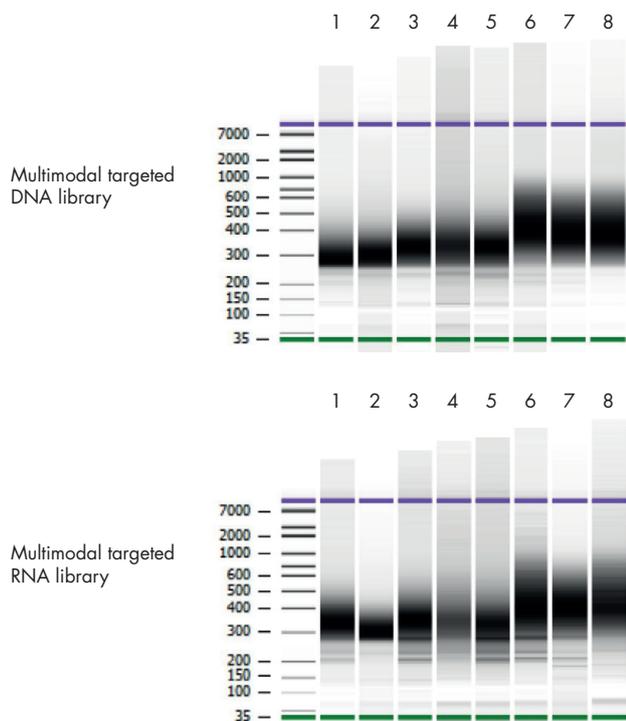
**Table 1: Biomarker types interrogated by the QIAseq Multimodal Panels**

<b>Biomarkers from DNA</b>	Single nucleotide variants (SNVs)
	Insertions and Deletions (InDels)
	Copy number variants (CNVs)
	Tumor mutational burden (TMB) score
<b>Biomarkers from RNA</b>	Microsatellite instability (MSI) loci
	Fusions
	Gene expression levels

**Figure 2. Convenient QIAseq Multimodal workflow.** Following isolation, nucleic acids (DNA and RNA) are enzymatically (for DNA) and heat (for RNA) fragmented. This is followed by DNA end-polishing and synthetic polyadenylation of RNA fragments. For library preparation, adapters containing UMIs are ligated to DNA molecules, and UMIs are added to RNA molecules during reverse transcription and template switch. Library fragments now serve as templates for DNA and RNA target enrichment using single primer extension. In this step, DNA and RNA targets are enriched using a single region-specific primer combined with a universal primer that contains the first of two sample indices. The final library amplification step ensures optimal sample amounts and adds the second sample index, creating a unique dual indexed library. The UDIs reduce the chance for index hopping during sequencing.

## Robust detection of DNA and RNA biomarkers

The QIAseq Multimodal Panels can be used to reliably detect DNA and RNA biomarkers using a consolidated workflow from total nucleic acids. The ability of QIAseq Multimodal Panels to simultaneously detect DNA and RNA biomarkers has been benchmarked using the following standards. For DNA verification, Quantitative Multiplex Reference Standard (FFPE) from Horizon was used, and for RNA verification, Seraseq FFPE Tumor Fusion Reference Material v2 from SeraCare was used. Tables 2 and 3 show the concordance between the Multimodal results and the expected results for biomarker detection on a NextSeq using 150 paired-end sequencing (300 cycles). Additionally, the QIAseq Multimodal Panels have been extensively validated against the QIAseq Targeted DNA Panels and QIAseq Targeted RNAscan Panels, demonstrating strong concordance (data not shown).



**Table 2. HD200 Variant Analysis.** Variants were called using the QIAseq Multimodal data analysis pipeline. All variants, as low as 1% VAF, were called as expected

Chromosome	Gene	Variant	Expected frequency (%)	Experimental frequency (%)
7q34	BRAF	V600E	10.5	7.0
7p12	EGFR	$\Delta E746-A750$	2.0	1.0
7p12	EGFR	L858R	3.0	3.2
7p12	EGFR	T790M	1.0	1.0
7p12	EGFR	G719S	24.5	24.6
12p12.1	KRAS	G13D	15.0	17.5
12p12.1	KRAS	G12D	6.0	7.4
1p13.2	NRAS	Q61K	12.5	13.1
3q26.3	PIK3CA	H1047R	17.5	17.1

**Table 3. SeraCare Fusion Analysis.** Fusions were called using the QIAseq Multimodal data analysis pipeline. All fusions were called as listed below, including two exon skipping events

	Detected using QIAseq Targeted RNAscan Panel	Detected using QIAseq Multimodal Panel
SIC45A3-BRAF	✓	✓
TMPRSS2-ERG	✓	✓
TPM3-NTRK1	✓	✓
PAX8-PPARG	✓	✓
NCOA4-RET	✓	✓
KIF5B-RET	✓	✓
FGFR3-TACC3	✓	✓
FGFR3-BAIAP2L1	✓	✓
SLC34A2-ROS1	✓	✓
ETV6-NTRK3	✓	✓
CD74-ROS1	✓	✓
EML4-ALK	✓	✓
EGFR exon skipping	✓	✓
MET exon skipping	✓	✓

**Figure 3. High-quality libraries.** The following libraries were analyzed: libraries 1–5 prepared from FFPE samples, library 6 prepared from HD200 Quantitative Multiplex Reference Standard FFPE (Horizon™), library 7 prepared from Seraseq® FFPE Tumor Fusion Reference Material v2 (SeraCare®) and library 8 prepared from HT 1080 cells. All libraries were of the expected size.

## Ordering Information

Product	Contents			Cat. no.
QIAseq Multimodal Panel (12)	Kit containing ALL reagents (except indices) for multimodal (DNA and RNA) sequencing; to process 12 samples	<b>Panel name</b>	<b>Panel variant number</b>	333932
		Sarcoma	UHS-003Z-12	
		Lung Cancer	UHS-005Z-12	
		Leukemia	UHS-009Z-12	
QIAseq Multimodal Panel (96)	Kit containing ALL reagents (except indices) for multimodal (DNA and RNA) sequencing; fixed small panel to process 96 samples	<b>Panel name</b>	<b>Panel variant number</b>	333935
		Sarcoma	UHS-003Z-96	
		Lung Cancer	UHS-005Z-96	
		Leukemia	UHS-009Z-96	
QIAseq Multimodal Custom Panel (96)	Kit containing ALL reagents (except indices) for multimodal (DNA and RNA) sequencing; Custom panel to process 96 samples			333955
QIAseq Multimodal Index I (12)	Box containing indices, enough to process a total of 12 samples, for indexing up to a total of 12 samples for QIAseq Multimodal Panel sequencing on Illumina platforms			333962
QIAseq Multimodal Index I Set A (96)	Box containing indices, enough to process a total of 96 samples, for indexing up to a total of 48 samples for QIAseq Multimodal Panel sequencing on Illumina platforms; one of two sets required for multiplexing 96 samples			333965
QIAseq Multimodal Index I Set B (96)	Box containing indices, enough to process a total of 96 samples, for indexing up to a total of 48 samples for QIAseq Multimodal Panel sequencing on Illumina platforms; Two of two sets required for multiplexing 96 samples			333975

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