#### Service Profile

## Multimodal Cancer Genomics Profiling Services

### Helping you target cancer with an all-in-one solution

Recent advances in tumor profiling and biomarker research have revealed that both DNA and RNA alterations can contribute to cancer progression. It is therefore becoming increasingly important to analyze multiple analytes from the same sample in a multimodal fashion. However, limited sample availability, complex workflows and high investments in time and money make multimodal analysis challenging.

QIAGEN Genomic Services overcomes these limitations by combining our optimized, multimodal panels with expert data analysis to support your cancer profiling needs. Extend your in-house resources with the expertise, powerful bioinformatics and custom services that you expect from QIAGEN®. Our all-in-one profiling solution offers the following benefits:

- End-to-end service: we take care of every step, from sample preparation to data analysis
- Complete multimodal workflow: we assess DNA and RNA alterations, tumor mutational burden (TMB) and microsatellite instability (MSI) from a single sample
- Twenty years of curated findings and interpretations: we offer highly-confident variant calling and interpretation summaries that include the latest biological, diagnostic, prognostic and therapeutic evidence
- Comprehensive reports and raw data: we enable the possibility for further downstream analysis and development
  of an internal database
- Full-spectrum solution: we provide a seamless flow from biomarker discovery to clinical assay development and approval

Partner with us for expert guidance and dedicated service – from Sample to Insight – for profiling your samples today.

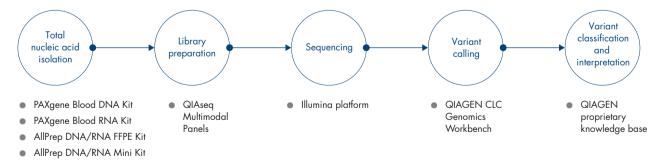


Figure 1. Sample to Insight multimodal cancer genomics workflow.



### One efficient workflow for confident detection of low-frequency variants

Our QlAseq® Multimodal Panels use single primer extension (SPE) technology to overcome the limitations of two-primer amplicon approaches on amplicon size and primer multiplexing. Plus, we incorporate both unique molecular indices (UMIs) and unique dual indices (UDIs) during library preparation to enable highly sensitive variant detection while reducing index hopping and read mis-assignment.

We offer cancer genomics profiling based on four distinct multimodal panels (pan-cancer, lung, leukemia and sarcoma) to best suit your unique research needs. As an example, our QIAseq Multimodal Pan-cancer Panel targets 523 genes and 56 RNA fusions implicated in the tumorigenesis of solid and heme malignancies, plus 26 key loci associated with MSI status, enabling an assessment of key immunotherapy biomarkers. And by covering >1 Mb of the genome, this panel can provide a statistically significant evaluation of TMB.

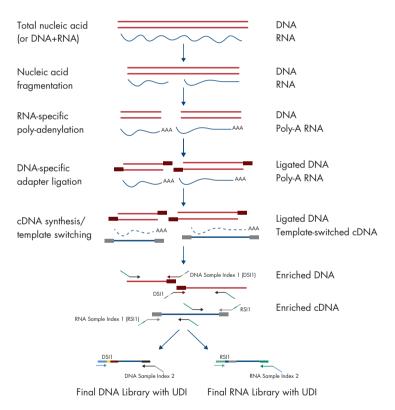


Figure 2. QIAseq Multimodal Panels workflow, using combined targeted DNA and RNA enrichment.

## An expert-curated interpretation summary of your profiling results - delivered

Using our cutting-edge bioinformatics tools in QIAGEN CLC Genomics, including built-in systems for DNA and RNA analysis and pre-optimized TMB and MSI workflows, we provide you with detailed sequencing reports. In addition, our professional interpretation service, powered by a team of molecular biologists and oncologists, provides a comprehensive analysis of each of your variants. To meet your research needs, we examine your variants in the context of their cancer sub-type, including information on the mutations' molecular characteristics, roles in disease and associated therapeutic, prognostic and diagnostic relevance.



# Get up-to-date insights

Our team of experts extracts the latest biological, diagnostic, prognostic and therapeutic evidence for your variants from the QIAGEN Knowledge Base, representing more than 20 years of curated findings and interpretations.



Leave the heavy-lifting to us

For rare or novel variants, QIAGEN's expert MDs and Ph.D-qualified scientists perform in-depth research, curation and interpretation for you.

#### Make your next discovery faster

- √ Manually-curated interpretation summary
  - Every sentence backed up with references
- ✓ Expert classification according to AMP guidelines
- ✓ SNVs, indels, fusions, CNVs, MSI and TMB
- √ Variant-level molecular impact
- √ Variant- and disease-specific relevance reviewed by medical oncologists
- ✓ Multivariant analysis
  - Effect of co-occuring variants
- √ Guideline summary

 $Figure \ 3. \ The \ benefits \ of \ our \ decision-ready, \ variant- \ and \ disease-specific \ interpretation \ services.$ 

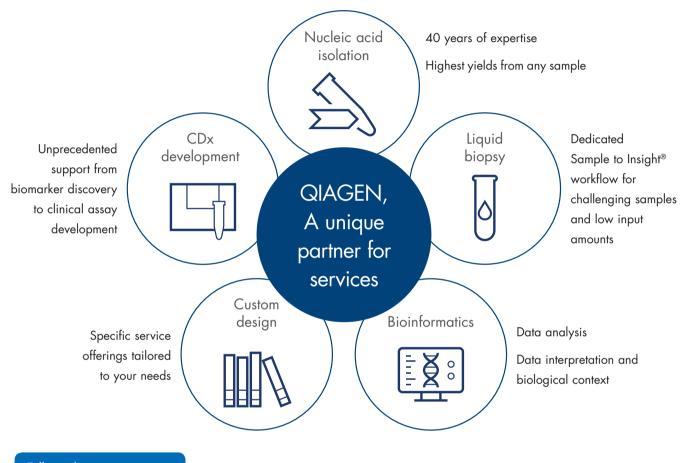
# Service specifications

Consultation VI	Free consultation with an expert to desig	gn an experimental setup that best mee	ets your needs and budget.
	Input sample	Isolation kit	Input requirements
Sample requirements	Customer-isolated DNA and RNA (total nucleic acid or separately isolated)	Not applicable	Minimum DNA: 150 ng (>10 ng/μl) Minimum RNA: 550 ng (>35 ng/μl) Minimum FFPE DNA and RNA: each 600 ng (>45 ng/μl)
	FFPE samples	AllPrep® DNA/RNA FFPE Kit	Maximum: 4 sections (10 µm,150 mm²) or 2 sections (20 µm,150 mm²)
	Whole blood	PAXgene® Blood DNA Kit PAXgene Blood RNA Kit	2 tubes
	Tissue	AllPrep DNA/RNA Mini Kit	Minimum: 10 mg Maximum: 30 mg
	Cells	AllPrep DNA/RNA Mini Kit	Minimum: 1 x 10 <sup>6</sup> cells pelleted and frozen Maximum: 1 x 10 <sup>7</sup> cells pelleted and frozen
	Other	Please inquire	
	RNA	DNA	FFPE samples
Sample quality control	Fluorescence-based dye for quantification (Capillary) gel electrophoresis (e.g., RIN value)	Fluorescence-based dye for quantification (Capillary) gel electrophoresis (e.g., DIN value)	RNA: fluorescence-based dye for quantification, (capillary) gel electrophoresis (e.g., DV200) DNA: fluorescence-based dye for quantification, QIAseq DNA QuantiMIZE Kit
	This is a <b>STOP/GO</b> point where it is possible to omit samples, replace samples before proceeding or terminate the project.		
Library preparation and quality control	Library preparation is performed using the following multimodal panels: High-content panels are assessed using the QIAseq Pan-cancer Multimodal HC Panel.  Non-high-content panels are assessed using the QIAseq Lung Multimodal Panel, QIAseq Leukemia Multimodal Panel, or QIAseq Sarcoma Multimodal Panel.  Unique molecular indices (UMI) are incorporated.	2. Library quality control (QC) is assessed by gel electrophoresis to check for the right fragment size and concentration.  Library quantification is assessed by qPCR.  We will notify you about the QC results.  This is a STOP/GO point where it is possible to terminate or adjust before proceeding.	3. Separated targeted DNA and RNA enrichment is carried out for maximal panel specificity (QIAseq Pan-cancer Multimodal HC Panel only, separated enrichment).  Combined targeted DNA and RNA enrichment is carried out for maximal detection sensitivity of DNA and RNA variants (only on request).
DNA sequencing parameters	Sequencing with Illumina® NextSeq®500, NextSeq550, MiSeq® or NovaSeq™ systems.  Paired-end reads, 2 x 150 bp.  For recommended read allocations for cataloged QIAseq multimodal libraries, please refer to the appropriate handbook.		

Complete data analysis	Raw data	De-multiplexed FASTQ files	
	Raw data QC	CLC graphical QC report (per sample)	
		CLC supplementary QC report (per sample)	
	Data trimming	CLC trim report (per sample; removal of adapters, low-quality, short sequences and ambiguous nucleotides)	
	DNA mapping (GRCh38)	UMI groups report (per sample; reads collapsed by UMIs)	
		Coverage report (per sample)	
		Per region statistics track (per sample; coverage levels of targeted regions in the pane	
		Indels and structural variant report (per sample; statistics of the mapping of unaligne read ends)	
	RNA mapping and quantification (GRCh38)	UMI groups report (per sample)	
		RNA-seq report (per sample)	
		Fusion gene report (per sample)	
		RNA primer report (per sample; QC metrics including how many genes were being targeted, target coverage)	
		Counts matrix (including read count, UMI count, mean reads per UMI, total gene reads, expression value, TPM normalized counts)	
		Combined report (per sample; an overview of all the metrics described above)	
	Variant calling	Variants list (per sample; single and multi-nucleotide variants (SNV, MNV); insertions and deletions; fusion genes)	
	Interpretation report	Combined alteration report, including DNA alterations, fusions, CNV, TMB, and MSI (per sample)	
	Data delivery	Encrypted USB/hard disk drive or cloud delivery	
Final report and consultation	The final data analysis package contains an overview of data analysis and algorithms used, the files and tables listed above and publication-ready figures (PDFs provided as standard, please inquire for SVG or other formats). A teleconference is scheduled with QIAGEN scientists to discuss analysis and validation of results. Consultation and support will be provided for 90 days following delivery of data (for data delivery only projects), or delivery of data		

## How can we accelerate your research?

Our expert team is looking forward to learning about your research project and designing your customized service with QIAGEN.



Tell us about your project

The QIAGEN Genomics Profiling Service is intended exclusively for research use only (RUO). This service is not intended for the diagnosis, prevention or treatment of a disease.

For up-to-date licensing information and product-specific disclaimers, see the respective QIAGEN kit handbook or user manual. QIAGEN kit handbooks and user manuals are available at **www.qiagen.com** or can be requested from QIAGEN Technical Services or your local distributor.

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