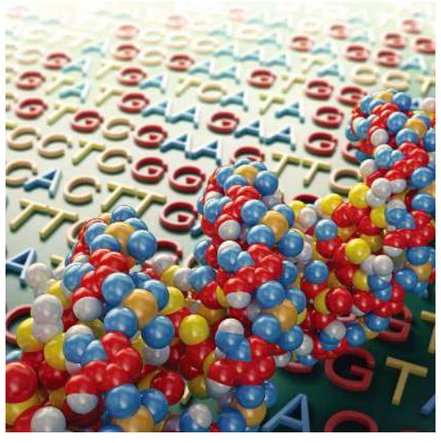
Targeted Sequencing Overview

Celemics has developed and delivered over 1,000 different customized panels. Our target enrichment method is capable of specifically isolating your genomic loci of interest out of the whole genome and increasing the sensitivity of detecting genetic mutations by producing higher coverage & in-depth sequencing data.

END-TO-END CUSTOMIZATION



PANEL DESIGN

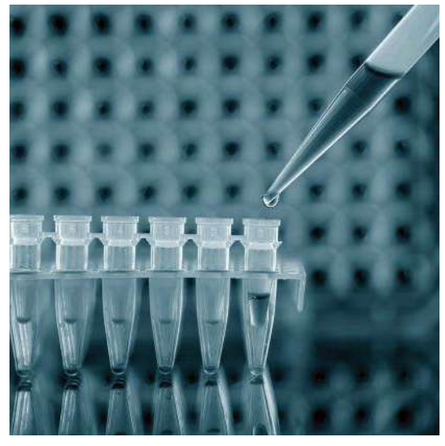
- Elaborately designed NGS panels comprised of your genes of interest
- Interactive discussion with customer prior to designing the panel (e.g., GC-rich, Homologous regions)
- Supported by advanced technology for probe design and reagent optimization
- Panel expansion possible through simple gene addition
- Alternative protocols in case required instruments are not available

SUPERIOR PERFORMANCE

- Market leading target enrichment kits
- Maximized cost-effectiveness
- Pre-capture pooling and high panel performance enables additional cost and labor savings

IN-HOUSE TEST & REBALANCING

- Adjustments to performance and functionality through thorough in-house validation test for every designed panel
- Detailed QC results encompassing wet-lab experiments, NGS run, and bioinformatics analysis provided to customer
- Rebalancing service possible through request
- Able to increase depth and coverage of a specific area if requested
- Finalize your order after reviewing QC results



DATA ANALYSIS

- Technical support available for customers new to NGS analysis
- Provides bioinformatics analysis services and tools from FASTQ to clinical report by request

OUTSTANDING PERFORMANCE OF TARGETED SEQUENCING

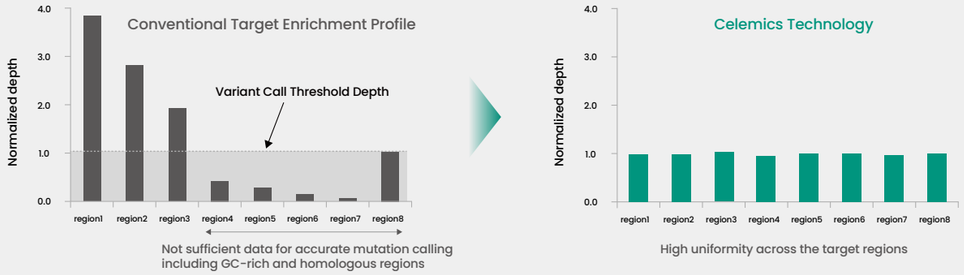
At Celemics, we support our customers through target hybridization-based NGS services and products individually designed and manufactured by experienced researchers and technicians. We have established a robust system for customized design panels and developed a variety of kits according to our customer's needs. All Ready-to-Use kits are completely validated and provide the best performance in the market. Our research team has designed and manufactured over a thousand customized panels and promises to offer the best quality product and service to our customers.

Key Features

1. Exceptional panel performance achieved by hybridization-based target capture method	Overcome limitations of amplicon-based NGS analysis with thoroughly validated hybridization-based target capture method High uniformity and coverage achieved by Celemics proprietary probe design technology
2. Assess all types of mutations with high sensitivity and specificity	Superior analytical performance compared to competitor products in detecting SNV, InDel, CNV, and rearrangement in a single NGS run with maximized sensitivity and specificity and minimized NGS noise enabled by Celemics unique molecular barcode assay and robust bioinformatics pipeline
3. Robust performance of assessing DNA and RNA across various specimen quality	Compatible with poor-quality and low-amount specimens such as FFPE, solid tumor, liquid biopsy, etc.
4. Efficient capture of 'Hard-to-Capture' regions	Analyze the clinically significant mutations embedded in GC rich or homologous regions, which are frequently masked by competitors
5. Wide compatibility with NGS instruments and automation platforms	Compatible with all NGS Instruments from Illumina, Thermo Fisher Scientific, Pacific Bioscience, MGI, and Oxford Nanopore Provides enzymes for DNA fragmentation as a substitute for sonicators
6. Flexible panel content: number of reactions of your choice and Gene Add-on Service	Save costs by ordering the number of reactions required for your experiment Expand your panel with minimum cost, time, and effort by simply adding or combining panels and genes of your interest

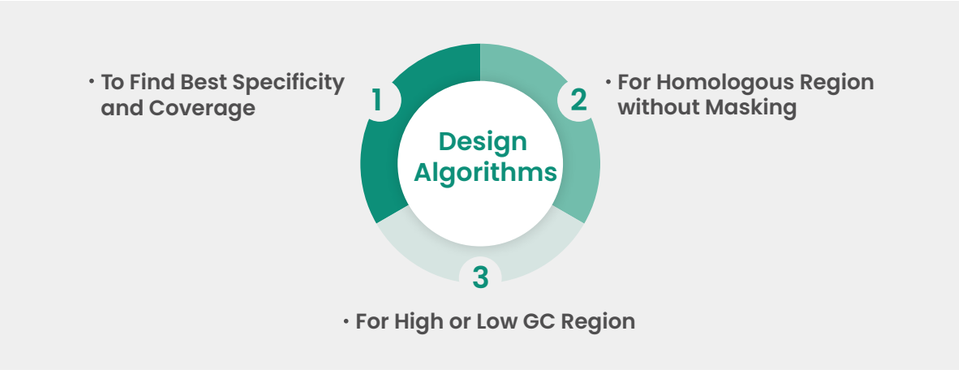
PROBE DESIGN TECHNOLOGY

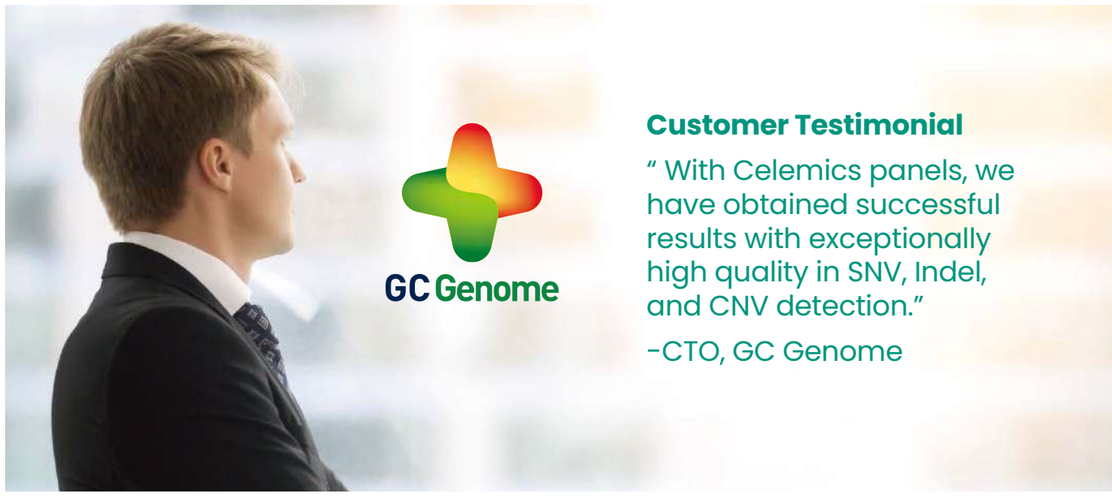
Market Problem and Celemics' Answer



Proprietary Probe Design Algorithm

Based on extensive wet-lab target capture experimentation for every customized panel



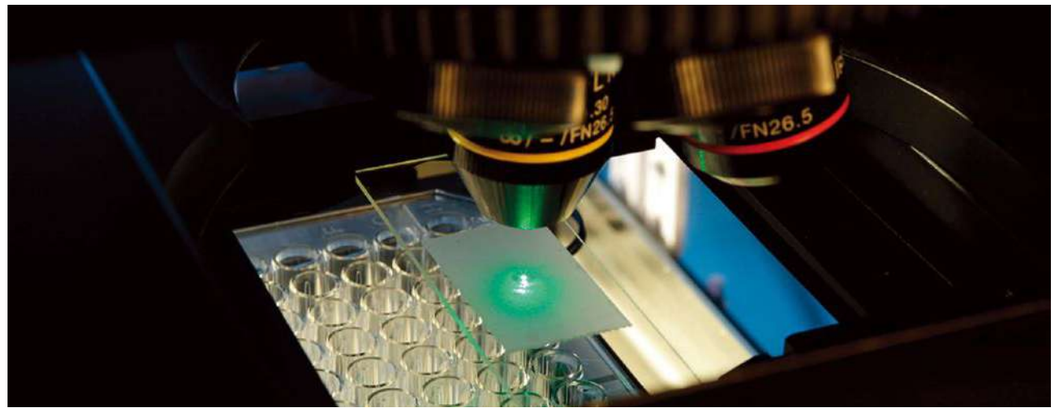


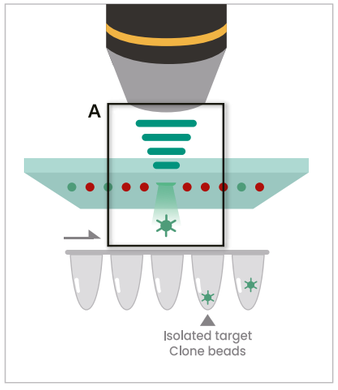
PROBE DESIGN TECHNOLOGY

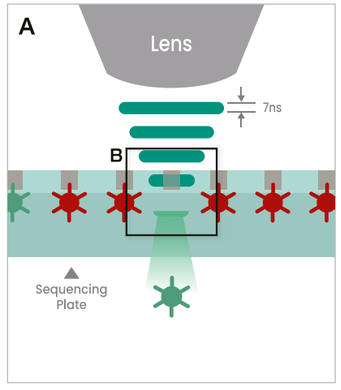
Proprietary Probe Manufacturing Technology

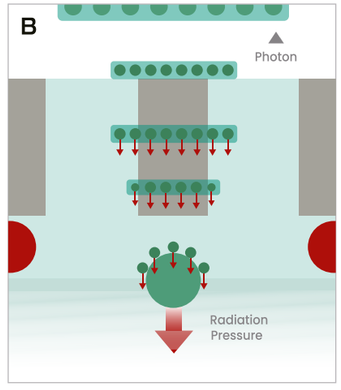
- Reduces complexity in handling complex oligo pools
- Enables extremely low-biased probe pool with handling individual probe sets
- Allows for cost-effectiveness and high-performance: advantage from pool-based probes and individually synthesized probes
- Achieves superior lot-to-lot uniformity for repeated orders due to proprietary 2-step probe synthesis technology

MSSIC Technology: Massively Separated and Sequence Identified Cloning

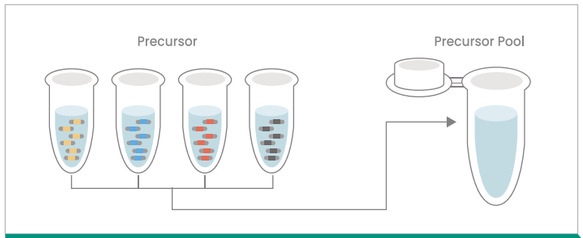




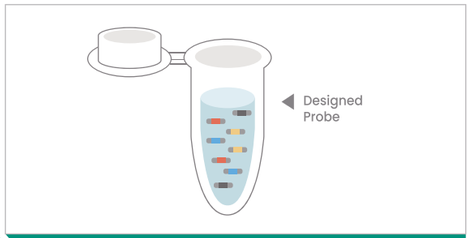




Two step probe manufacturing



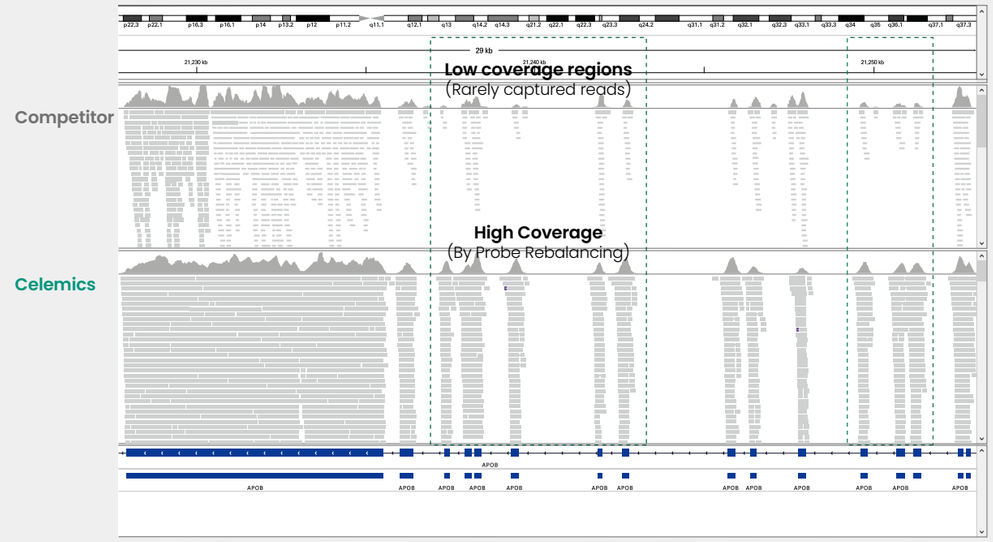
STEP 1. Manufacturing and Pooling of Precursor



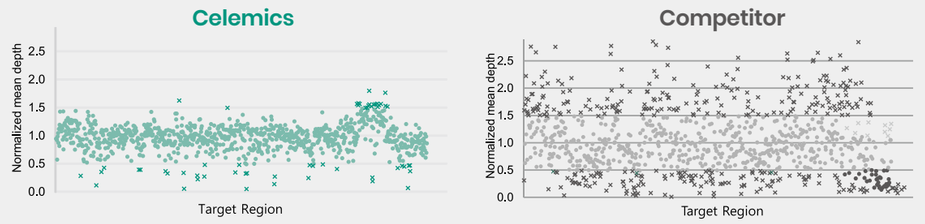
STEP 2. Optimized NGS Panel

TARGETED SEQUENCING PANEL PERFORMANCE

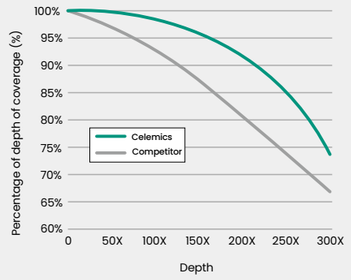
1. High Coverage Panel Compared to Competitor Products



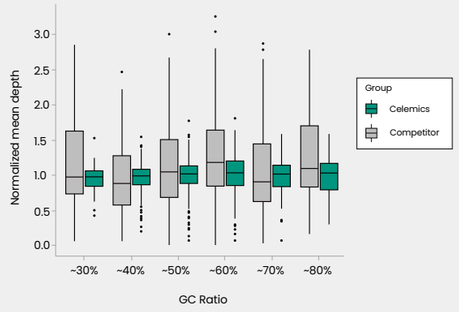
2. Higher Uniformity Across Target Regions



3. Superior Coverage Depth Over Target Regions



4. Superior Capture Performance Across GC Percentage

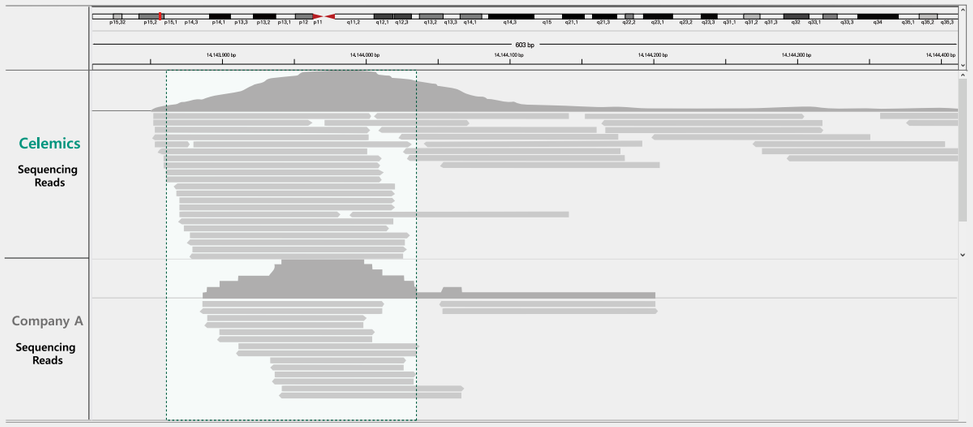


** Target region of both panels (BED file) are identical.
** Number of reads are the same for the results from both panels.

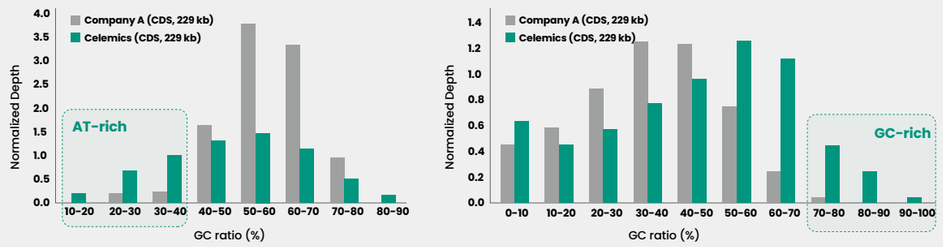
Targeted sequencing allows for sequencing with higher accuracy by specifically targeting the genomic regions of interest. The optimization process of the probes and reagents is essential for each of the different NGS platform types. Celemics has established the design technologies for the probes and reagents for various applications and achieved superior uniformity and depth of coverage compared to competitor products.

SEQUENCING PERFORMANCE OF CELEMICS PANEL FOR HARD-TO-CAPTURE REGIONS

1. Higher Depth compared to Company A Targeting Against the Same Target Area



2. Better Uniformity across AT- and GC-rich Regions

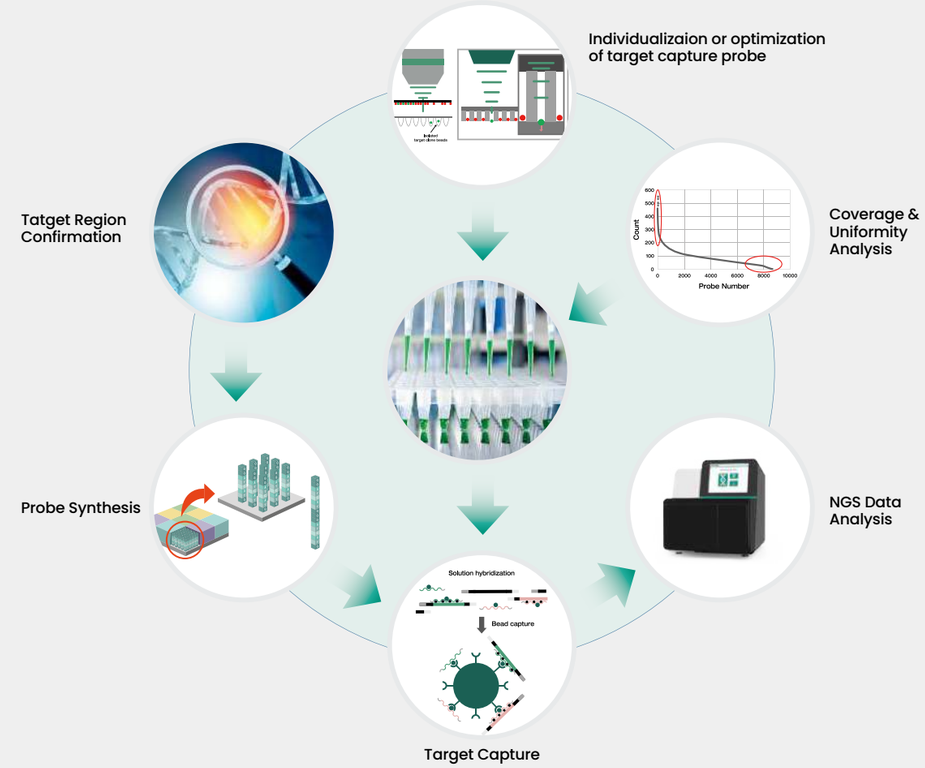


Even the most advanced NGS techniques have been challenged by GC-rich and homologous regions that are often masked or omitted by competitor services. Such a challenge is overcome by Celemics proprietary probe design technology which enables successful sequencing of GC-rich, AT-rich or homologous regions upon request. We also provide Homolog Report when the requested region includes homologous regions. Customers can then decide whether to include the regions in the order.

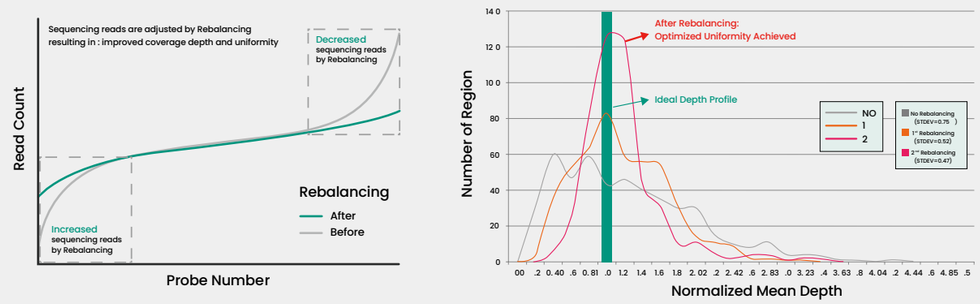
Our customers performed validation tests comparing Celemics' customized panels with our competitors'. For the competitor product, they performed validation tests based on competitor's recommended protocols for the same target regions. They also used the same sequencing amount for the fair experiment. As a result, customers selected our customized panels due to the high capture efficiency even with a lower amount of sequence data.

PILOT TEST & REBALANCING

Overview of Celemics Rebalancing Technology



Capture Uniformity Analysis



For customized targeted sequencing panels, we conduct in-house performance tests of requested panels and deliver the test results to customers. We also provide rebalancing services in case the customer requests for a specific area or overall performance improvement. The service includes redesigning probes against the requested regions and optimizing reagents to best meet our customers' needs.

EXAMPLE OF ctDNA ANALYSIS USING PROPRIETARY MOLECULAR BARCODES

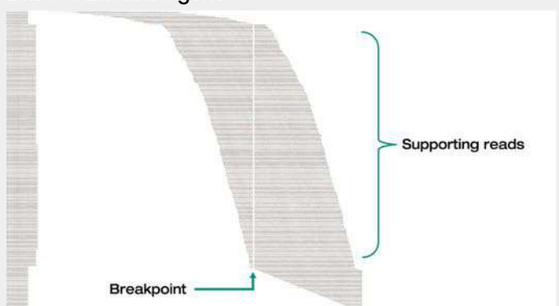
Performance Verification using Reference Material: 100% Sensitivity and Specificity

				0.5% VAF			1% VAF			WT		
	Gene	DNA change	AA change	VAF	VAF	VAF	VAF	VAF	VAF	VAF	VAF	VAF
Seracare	NRAS	c.182A>G	p.Q61R	0.96%	0.55%	0.78%	1.09%	0.98%	1.44%	0.06%	0.00%	0.00%
	PIK3CA	c.1633G>A	p.E545K	0.57%	0.69%	0.24%	1.18%	1.13%	0.38%	0.00%	0.00%	0.00%
	PIK3CA	c.3140A>G	p.H1047R	0.42%	0.33%	0.45%	0.81%	0.93%	0.94%	0.00%	0.00%	0.00%
	PIK3CA	c.3204_3205insA	p.N1068fs*4	0.51%	0.45%	0.51%	0.86%	0.95%	0.87%	0.00%	0.00%	0.00%
	EGFR	c.2310_2311insGGT	p.D770_N771insG	0.38%	0.36%	0.42%	0.48%	0.86%	0.78%	0.00%	0.00%	0.00%
	EGFR	c.2369C>T	p.T790M	0.44%	0.48%	0.48%	0.77%	1.23%	1.05%	0.00%	0.00%	0.00%
	EGFR	c.2573T>G	p.L858R	0.56%	0.51%	0.74%	1.58%	1.39%	0.85%	0.00%	0.00%	0.00%
	BRAF	c.1799T>A	p.V600E	0.51%	0.52%	0.47%	0.78%	0.70%	0.45%	0.00%	0.00%	0.00%
	PTEN	c.741_742insA	p.P248fs*5	0.31%	0.55%	0.51%	1.16%	1.30%	1.52%	0.00%	0.00%	0.00%
	KRAS	c.35G>A	p.G12D	0.43%	0.34%	0.62%	1.16%	0.89%	0.91%	0.00%	0.00%	0.00%
	ATK1	c.49G>A	p.E17K	0.69%	0.37%	0.35%	0.65%	0.66%	1.01%	0.00%	0.00%	0.00%
	TP53	c.818G>A	p.R273H	0.40%	0.47%	0.41%	1.84%	1.14%	0.86%	0.03%	0.05%	0.00%
	TP53	c.743G>A	p.R248Q	0.47%	0.44%	0.50%	0.90%	0.88%	0.85%	0.02%	0.07%	0.00%
	TP53	c.723delC	p.C242fs*5	0.43%	0.40%	0.41%	0.87%	0.85%	0.72%	0.00%	0.00%	0.00%
	TP53	c.524G>A	p.R175H	0.71%	0.66%	0.71%	1.19%	1.13%	1.02%	0.06%	0.05%	0.03%
	TP53	c.263delC	p.S90fs*33	0.50%	0.81%	0.53%	1.31%	1.55%	1.37%	0.09%	0.01%	0.06%
			Avg. (%)	0.52%	0.50%	0.51%	1.04%	1.04%	0.94%	0.02%	0.01%	0.01%

Accurate CNV and Gene Rearrangement Analysis with FFPE Samples Due to High Coverage Uniformity

	Panel A (400 kb)		Panel B (2.2 Mb)	
CNV	100 ng	50 ng	100 ng	50 ng
MET	Detected	Detected	Detected	Detected
MYCN	Not in 400 kb panel target region		Detected	Detected

EML4 - ALK fusion gene



We have conducted complete validation test for each Ready-to-Use panel and proved its superior performance compared to competitor products. The products are highly optimized for accurate and efficient assays even with poor quality and low-amount samples such as FFPE, ctDNA, etc. As shown in the table above, we have successfully performed CNV and rearrangement analysis from 50 ng of FFPE samples.

COST-EFFECTIVE SEQUENCING

Significantly reduced cost in Sample Prep, Target Enrichment Kit, and Sequencing

1. Sample Prep consumables developed and provided by Celemics for the highest optimization include CeleMag™ Clean-up Bead, CeleMag™ Streptavidin Bead, CLM Polymerase, and EP-kit (one-step workflow from Fragmentation to End-repair and A-tailing).
2. Pre-capture pooling reduces costs per sample.
3. Celemics has secured technology for proprietary probe design and manufacturing, significantly reducing costs of our Target Enrichment Kit.
4. Celemics panels have shown superior performance compared to competitor product in terms of uniformity and on-target ratio, enabling high-quality, cost-effective sequencing.

CELEMICS FEATURES & BENEFITS

1. Hybridization-based capture	2. Maximized Efficiency allows Market Leading Capture Performance	3. Hybridization Enhancer Technology and Enzymatic Library Preparation
4. User-friendly Bioinformatics Software	5. Reduced NGS costs by Pre-capture pooling with no compromise on quality	6. Molecular barcode and bioinformatics for ultra-low VAF mutations
7. CAS for bioinformatics analysis	8. Flexible panel content with Gene Add-on Service	9. Default wet-lab QC for every customized panel
10. Minimal lot variation due to proprietary 2-step probe manufacturing technology	11. Compatible with all NGS instruments and automation platforms	12. Capture the 'Hard-to-Capture' regions
13. Optimization of species-specific blockers for maximum performance for agriculture and animal research	14. Improved Probe Design by Rebalancing Service only available in Celemics	15. Robust, Rapid, Reliable Customization

Targeted RNA Sequencing Panel

Transcriptome Analysis

KEY FEATURES

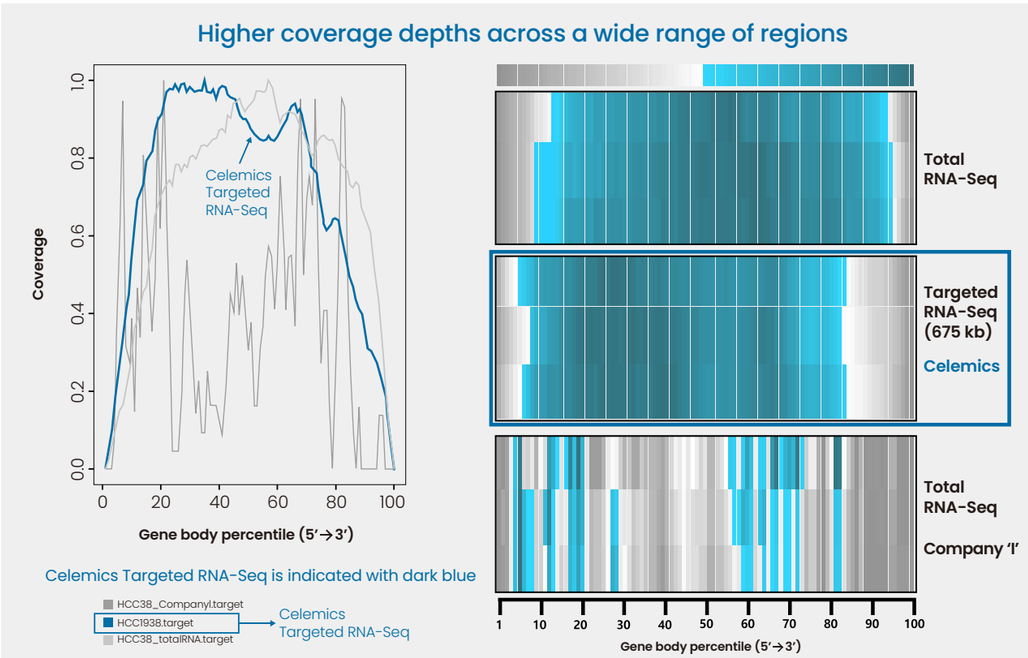
1. Cost-effective high-quality analysis	Accurate analysis of expression levels enabled by higher depth of coverage due to specific targeting of genes of interest, compared to total RNA sequencing
2. Compatible with a variety of sample types	Receive reliable results from poor-quality samples such as FFPE and low-amount samples such as cfRNA
3. Expression level in all regions of genes of interest	Covers all gene regions, allowing for the assessment of expression levels across all exons
4. Gene rearrangement analysis	Detects rearrangement and all other types of variants
5. Isoform analysis	Identify isoform expression levels by assessing the entire regions of targeted genes.

PACKAGE COMPOSITION

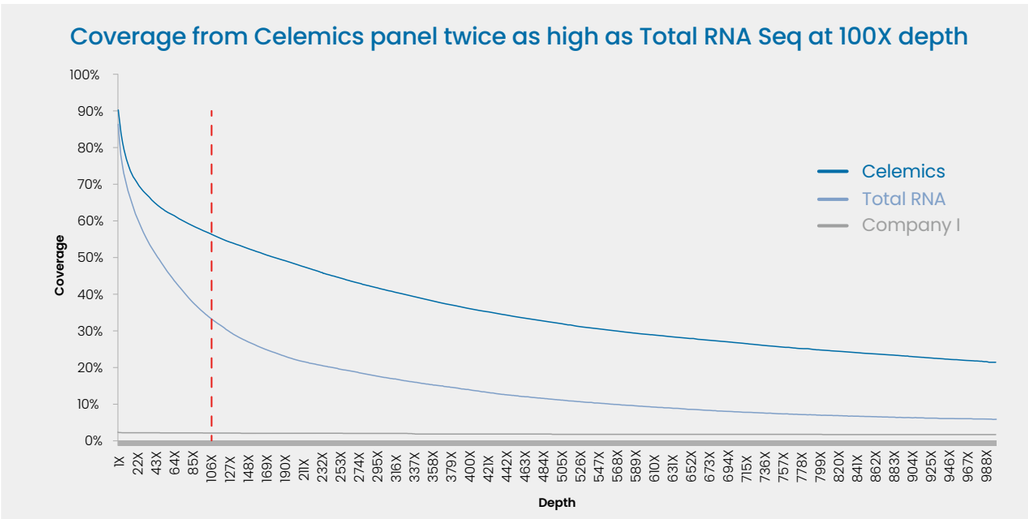
Package name	Compositions		
Target Enrichment	Target capture Probe	-	
Standard	Target Enrichment reagents	Library prep Kit	-
All-In-One			Beads / Polymerase

Package option	Options	
Pooling method	Single Reaction	Pre-capture Pooling
Library Preparation kits	Standard Kit	
Hybridization Enhancer	Included	Not included

PANEL PERFORMANCE



Celemics Targeted RNA Sequencing assesses the expression level of selective genes with sufficient level of coverage depth that is higher than that of total mRNA sequencing. Compared to competitor products that targets only parts of an exon, the Targeted RNA Sequencing developed by Celemics showed relatively higher coverage across a wide range of regions.



The comparison test between Celemics Targeted RNA Sequencing and total RNA sequencing shows that the coverage from the Celemics product is 15% higher at 50X and twice as high at 100X.

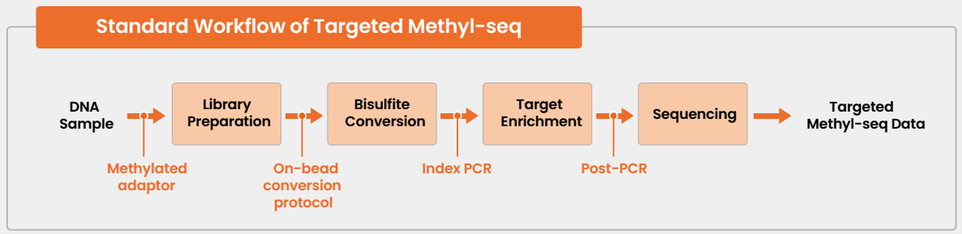
Targeted Methylation Sequencing Panel

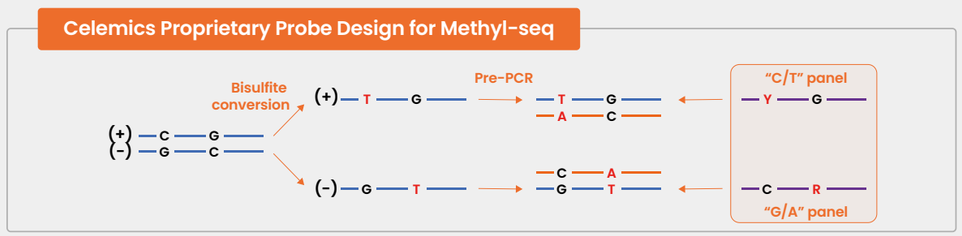
Epigenetics

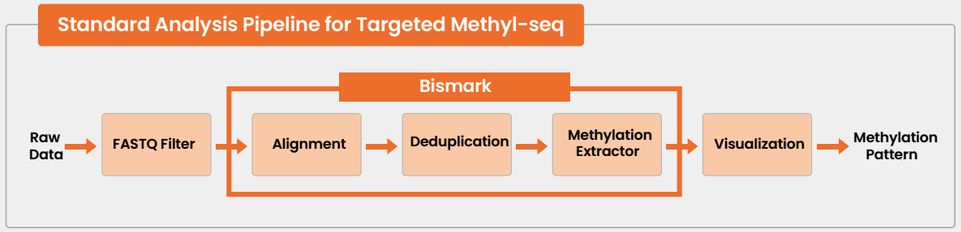
KEY FEATURES

1. Probe specifically designed for Methyl-seq	Elaborate design considering the sequence alteration by bisulfite conversion Thorough comparison analysis of the sequences before and after bisulfite conversion, enabling accurate detection of methylation sites
2. Compatible with all sample types	Perform methylation analysis with gDNA and cfDNA

PANEL PERFORMANCE

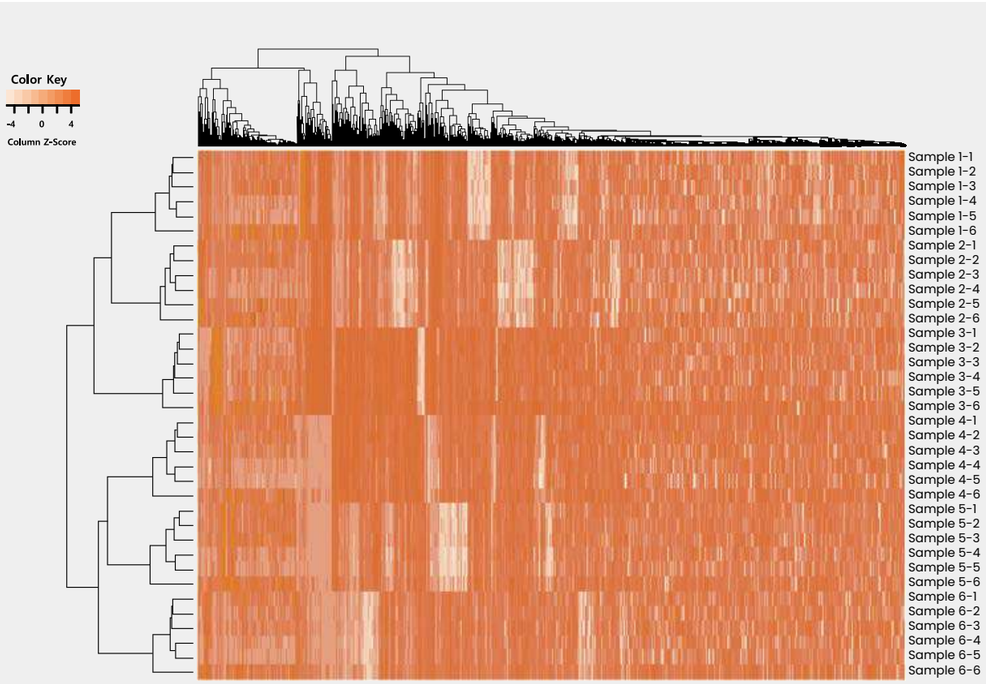






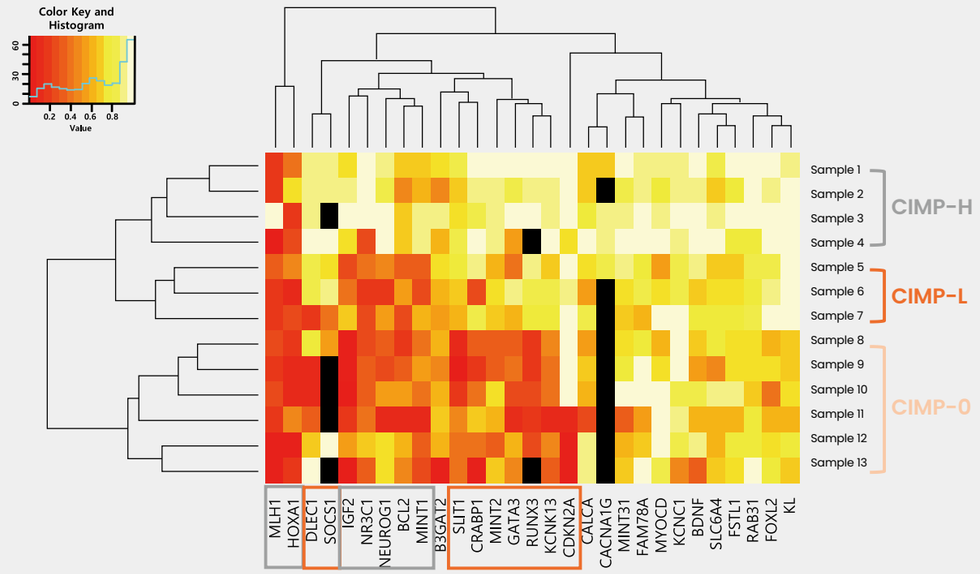
The Targeted Methylation Sequencing is proceeded with including a bisulfite conversion process in the NGS workflow.
The hybridization probe and methylated adapters are designed considering the sequence alteration by bisulfite conversion, enabling an accurate comparison analysis of the sequences before and after the conversion.
Selective genes are targeted for the analysis, allowing for cost-effective sequencing.

HIGH REPRODUCIBILITY OF METHYLATION PATTERN ANALYSIS



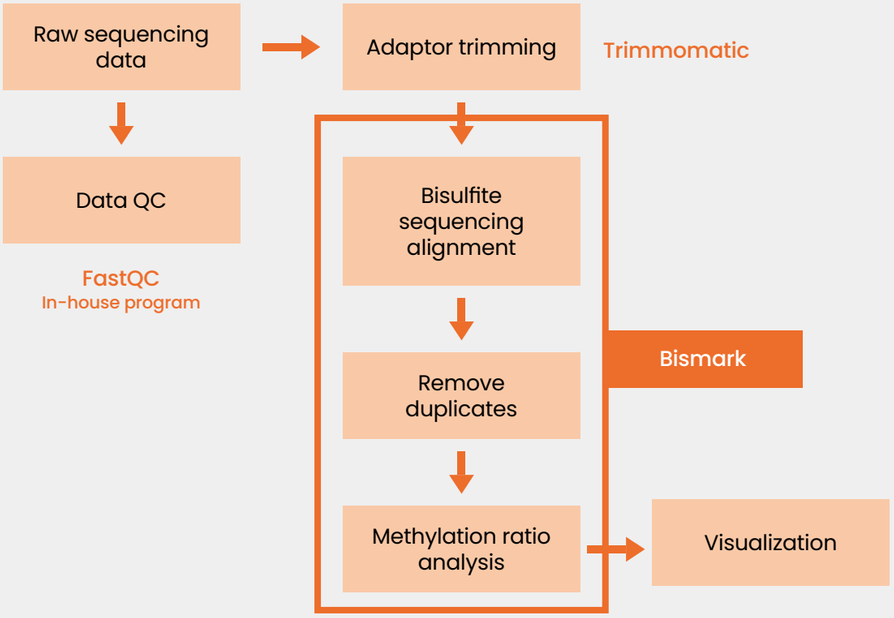
The results demonstrate high reproducibility of the analysis, yielding the same methylation patterns when repeatedly tested with the identical specimens.

HIGH CONCORDANCE OF METHYLATION PATTERN ANALYSIS WITH CLINICAL INFORMATION



The clustering result from pattern analysis showed high concordance with the clinical data information.

WORKFLOW OF TARGETED METHYLATION SEQUENCING ANALYSIS

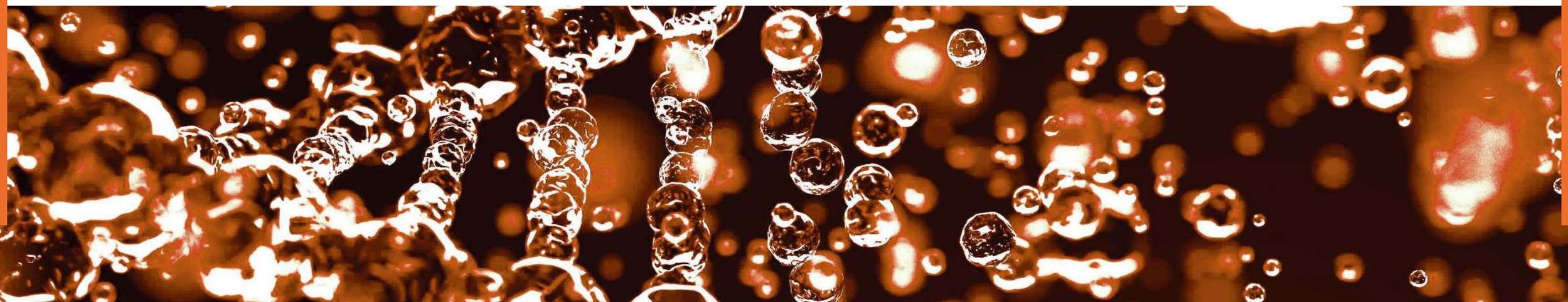


Customers who are new to methylation analysis are supported by Celemics bioinformatics software service for fast and accurate analysis.

PACKAGE COMPOSITION

Package name	Compositions		
Target Enrichment	Target capture Probe	-	
Standard	Target Enrichment reagents	Library prep Kit	-
All-In-One			Beads / Polymerase

Package option	Options	
Pooling method	Single Reaction	Pre-capture Pooling
Library Preparation kits	Standard Kit	EP-kit
Hybridization Enhancer	Included	Not included



Customized High-Throughput Genotyping Panel

Plant and animal research

DESCRIPTION

For molecular breeding, the availability and easy accessibility of genomic resources is a prerequisite. Although technological advances have provided a range of resources like molecular markers, genetic linkage maps, whole genome sequences and transcriptomes, agricultural genomics has faced many challenges. Celemics provides a solution with the High-Throughput Genotyping Panel. We have utilized NGS methods, whereby a high number of regions of interest are simultaneously enriched using specifically designed probes to provide new insights into different agricultural genomics research.

KEY FEATURES

1. NGS-based target enrichment sequencing assay	Utilize NGS-based target enrichment methods for higher accuracy and cost-effectiveness compared to conventional methods such as conventional GBS, PCR, and microarray
2. Comprehensive analysis with high accuracy	Perform comprehensive assay of 100 to 10,000 markers with minimized false-negatives and false-positives Discover novel SNPs
3. Cost-effective analysis	Benefit from Celemics' library preparation kits, target capture technology, and multiplexing indices specifically designed for high-throughput genotyping
4. Outstanding performance regardless of various origins	Receive high-quality results enabled by species-specifically designed blocking oligos across all types of origins

PACKAGE COMPOSITION

Package name	Compositions		
Target Enrichment	Target capture Probe	-	
Standard	Target Enrichment reagents	Library prep Kit	-
All-In-One			Beads / Polymerase

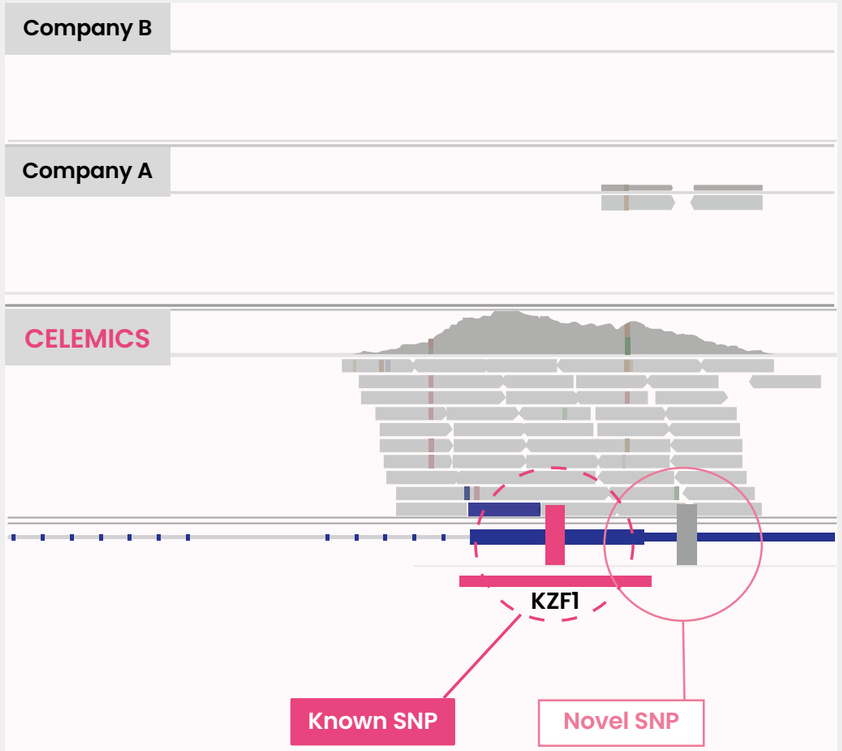
Package option	Options	
Pooling method	Single Reaction	Pre-capture Pooling
Library Preparation kits	Standard Kit	EP-kit
Hybridization Enhancer	Included	Not included

COMPARISON WITH CONVENTIONAL TECHNOLOGIES

	Advantages	Disadvantages
Conventional GBS	1. Sequencing of multiple samples due to lower amount of data required compared to WGS	1. Limited biomarkers available due to limited conserved regions, reducing overall resolution 2. Unable to detect SNPs in the restriction sites
Microarray	1. Higher reproducibility than conventional GBS	1. Hard to customize new targets (novel biomarkers) 2. Low flexibility to meet various kinds of genotyping
PCR	1. Cost-effective for low number of samples 2. Easy and fast analysis	1. Limited number of biomarkers to analyze at once 2. Inappropriate for mass-analysis of biomarkers
Celemics Target Enrichment	**1. Cost saving** : Highly cost-effective when assessing multiple samples **2. Flexible customization** : Novel biomarkers can be added or removed **3. Comprehensive analysis** : Including novel SNP discovery **4. Exceptional performance** : Celemics proprietary blocking oligo design technology **5. Wide compatibility** : Compatible with a wide range of sample types	

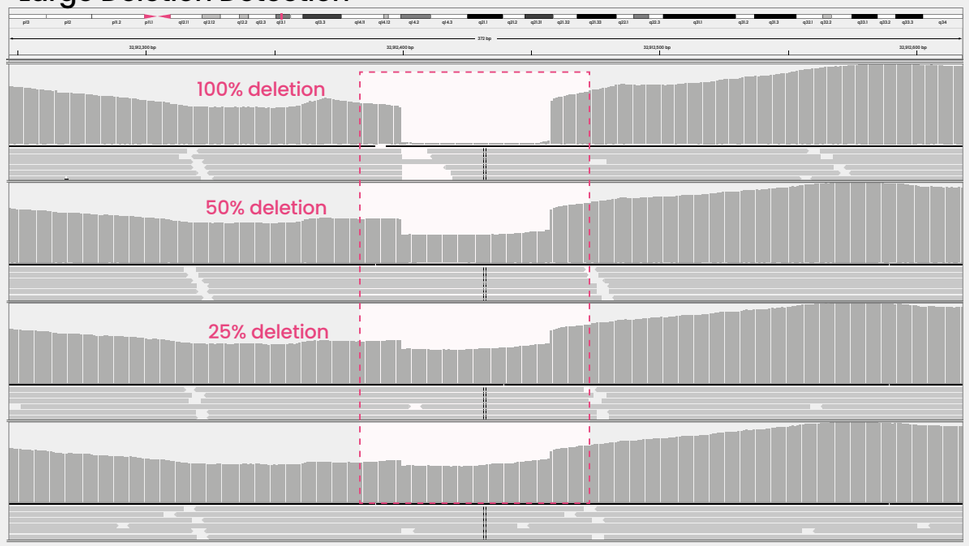
PERFORMANCE

Hybridization-based NGS target enrichment enables discovery of novel SNPs near target regions



PERFORMANCE

Hybridization-based NGS target enrichment enables accurate analysis of all mutation types including large deletion and rearrangement.



**Artificially generated data used*

Metagenomic Sequencing Service and Kit

16S V4 / 16S V3-V4 / 18S ITS1 / 18S ITS1-ITS2

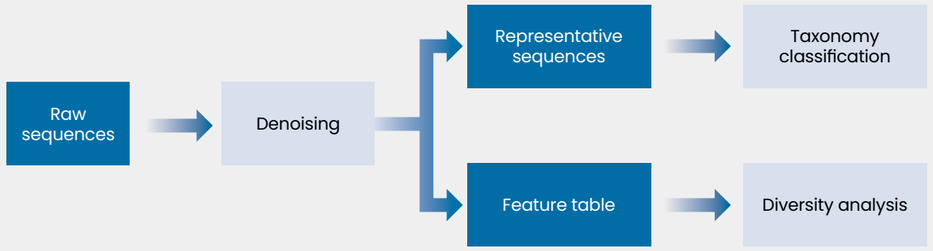
DESCRIPTION

Metagenomic Sequencing Service and Kit is used for microbiome and mycobiome studies. The service allows for characterizing and differentiating a myriad of microbial species. The 16S V4 (or V3-V4) region of bacteria and archaea and 18S ITS1 (or ITS1-ITS2) region of fungi is amplified by PCR. After cleaning up using CeleMag beads, the indices and adapters are attached for NGS and bioinformatics analysis. According to the purpose of customer's studies, various analysis reports are provided by the Celemics robust analysis pipeline. Please contact us for further information.

EXPERIMENT WORKFLOW

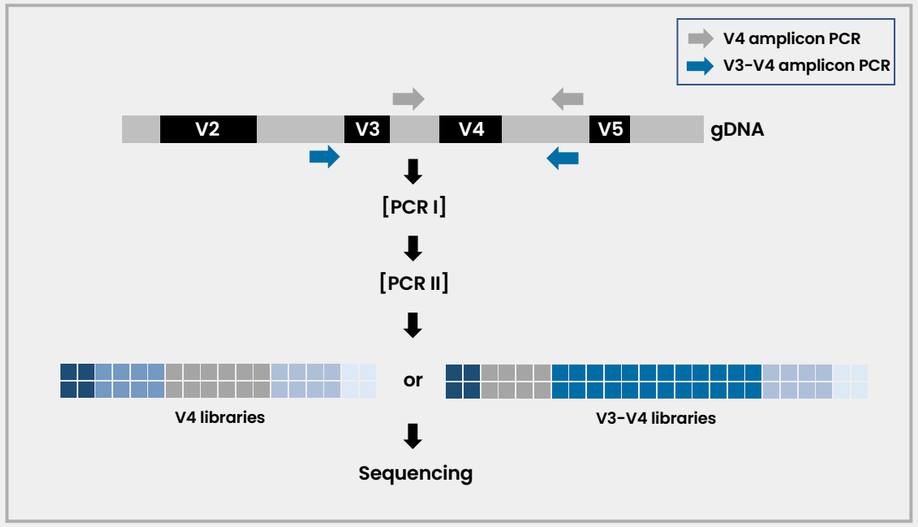
1. PCR amplification against gDNA using 16S region or ITS region specific primers
2. Bead cleanup
3. Index and adapter ligation with Nextera Index sets
4. Bead cleanup
5. Library pooling
6. NGS Sequencing

NGS-BASED METAGENOME ANALYSIS WORKFLOW

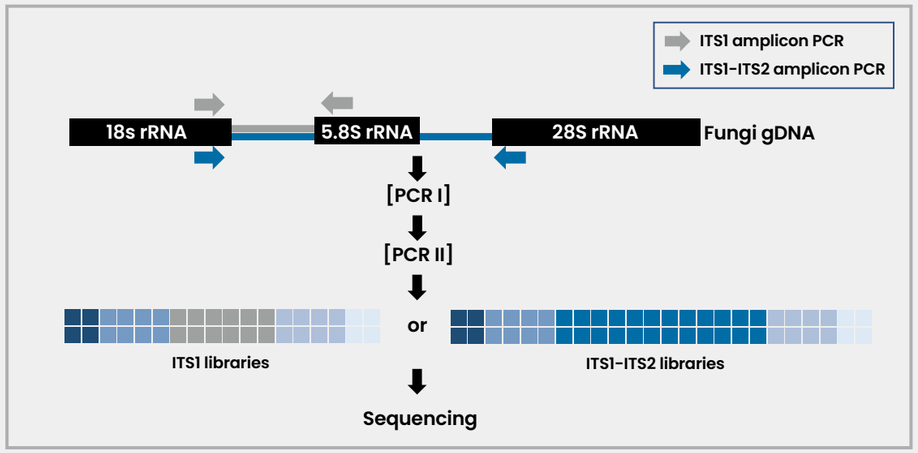


SEQUENCING WORKFLOW

16S rRNA V4 and V3-V4

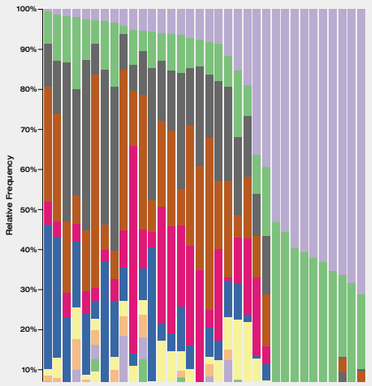


18S ITS1 and 18S ITS1-ITS2

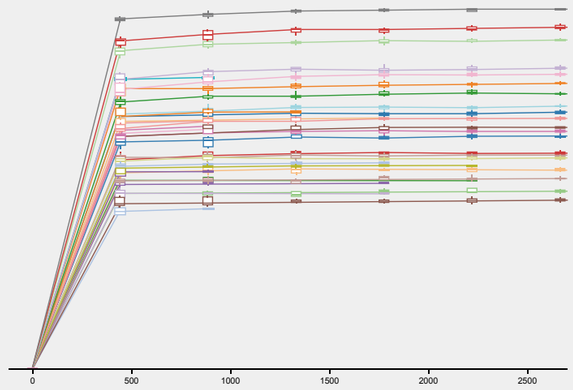


EXAMPLE OF METAGENOMIC SEQUENCING ANALYSIS REPORT

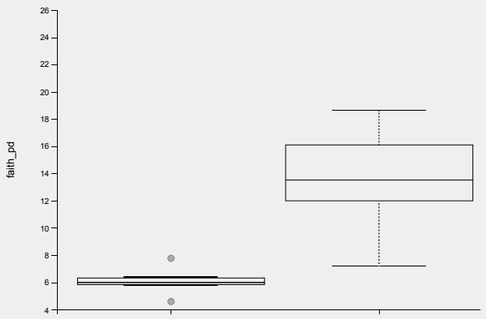
Taxonomy analysis



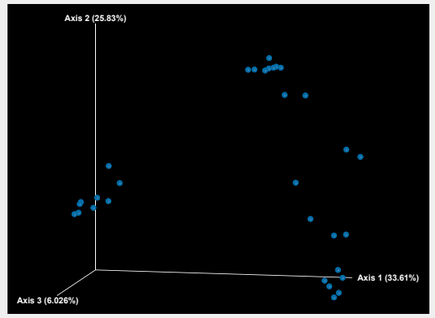
Alpha rarefaction



Alpha diversity



Beta diversity



Results presented above are a few selected examples of the metagenomics sequencing results that Celemics provides. Contact us for more information.