Celemics Whole Exome Sequencing Panel

Key Features

- **Complete Whole Exome Coverage**
- **Superior Performance in the Market**
- **Gene Add-On Service**
- **FASTQ to Clinical Interpretation Capability**
- **Rapid Same-Day Workflow**
- **No Need for Heavy Instruments**
- **Complete Walkaway Automation**
- **Flexible Integration with NGS Sequencers**

Celemics Whole Exome Sequencing (WES) Panel is a comprehensive solution that covers all target regions of major WES panels available in the market.

With a target size of 37.1 Mb, the panel does not compromise performance in terms of coverage and uniformity, enabling highly efficient and cost-effective sequencing of the human whole exome. The panel coverage spans across exon regions from RefSeq, CCDS, and GENCODE.

Celemics panels also perform well against hard-to-capture regions such as GC-rich regions. Regarding spike-in options, we have the ability to customize our WES panel according to your specific needs by including mitochondrial or intronic regions upon request.

The panel is also fully supported by Celemics Analysis Service (CAS), our end-to-end bioinformatics solution.

Complete Whole Exome Coverage

What differentiates the Celemics Whole Exome Sequencing Panel from other WES panels in the market?
Most researchers look for complete coverage especially when it comes to WES. However, most WES panels in the market vary in their target regions and some compromise with coverage, even deleting hard-to-capture regions in order to enhance performance. Celemics has developed a WES panel that covers the regions of all four major WES panels in the market, spanning the coding regions from RefSeq, CCDS and GENCODE. The Celemics WES Panel provides the most comprehensive coverage of protein-coding regions, thereby enabling marker discovery to diagnostics.

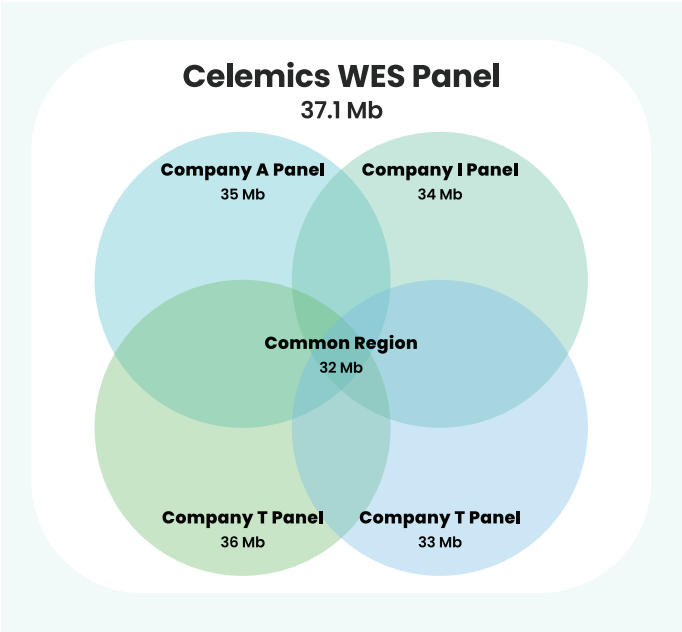

Figure 1. Complete Whole Exome

The Celemics WES Panel covers the target regions of all major whole exome panels in the market, which include WES panels from company A, company I and company T. Among the regions that Company A and T failed to cover from their own target regions, Celemics covers an additional 60 Kb and 306 Kb of Company A and T respectively (data not shown). Most of these regions are challenging to capture due to GC-rich and repeated sequences. Through Celemics' optimized probe design and panel synthesis technology, the Celemics Whole Exome Panel is able to successfully cover the challenging regions that other company products struggle with.

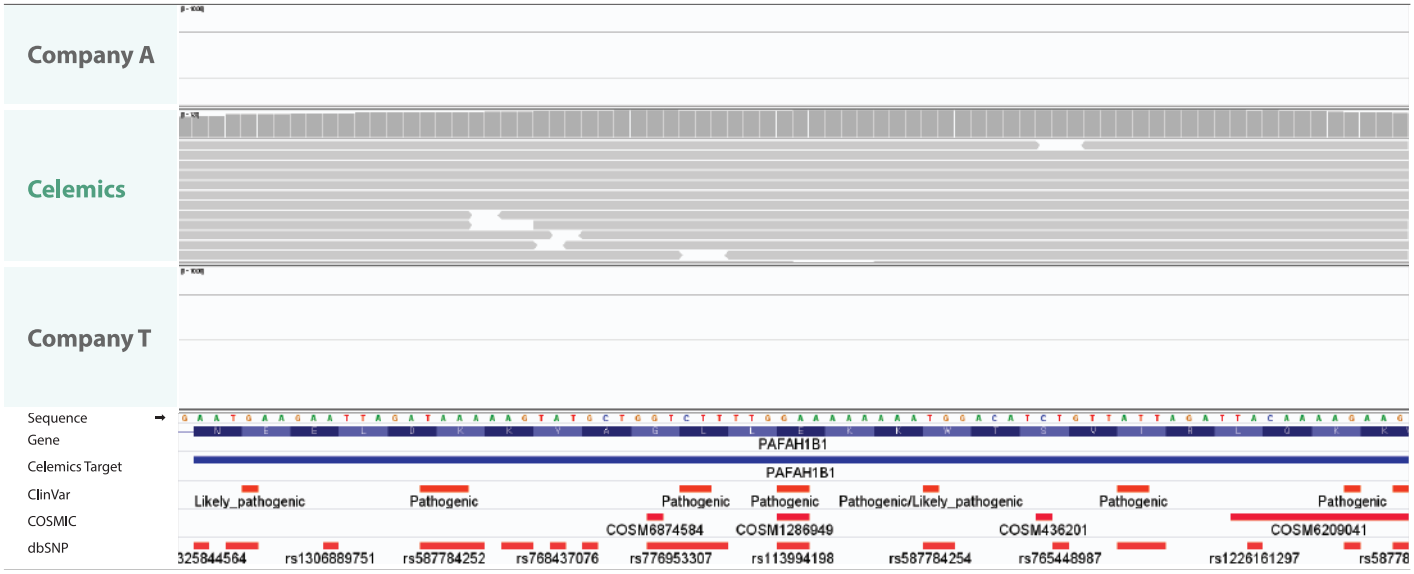

Figure 2. Superior Capture Performance and Coverage

A mutation in PAFAH1B1 causes Isolated Lissencephaly Sequence (ILS) & Miller-Dieker syndrome. While other competitor panels fail to capture the A-T rich regions in this gene, the Celemics WES Panel successfully covers the region.

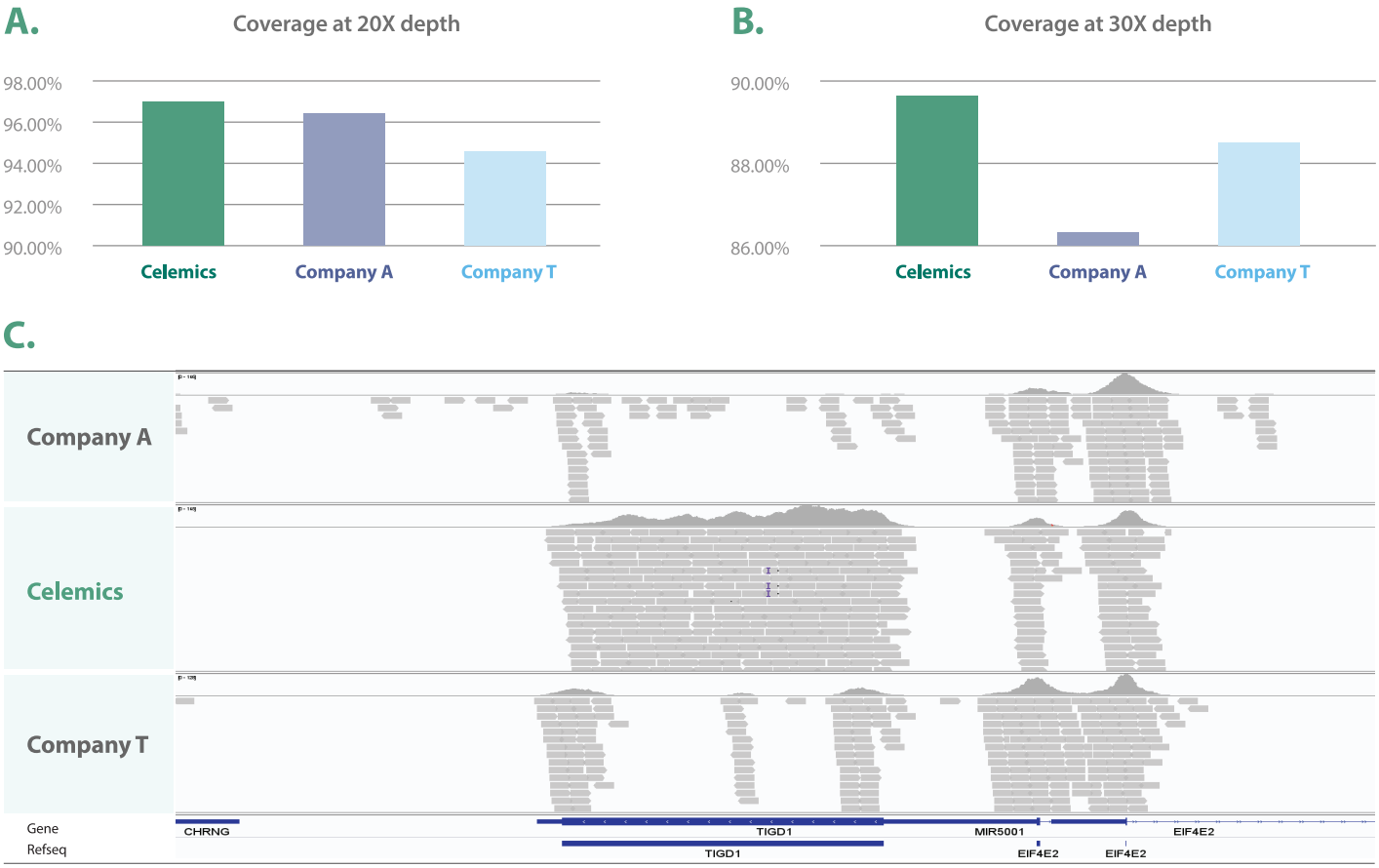

Figure 3. Exhaustive Coverage for Each Gene

The Celemics WES Panel covers each gene with thorough coverage in comparison to competitor products. The bar graphs indicate the percentage of genes that are covered at (A) 20X depth and (B) 30X depth. The data from the three panels were downsampled to 5.4 Gb. (C) The IGV figure demonstrates the superior coverage performance of the Celemics Whole Exome Panel against the TGID1 gene compared to other competitor products.

Exceptional Target Capture Performance

Celemics provides market-leading target capture performance due to probe design and reagent optimization technology. Despite some companies who resort to masking the hard-to-capture regions (such as GC- or AT-rich regions and homologous regions) or completely omit the regions from their target in order to enhance the result quality, Celemics provides both high coverage and on-target ratio without reducing the number of target regions. With Celemics' proprietary technology, the Celemics WES Panel captures regions that no other companies could capture with quality coverage and uniformity. The all-around performance of Celemics' WES panel, regardless of sample type, allows for highly sensitive, cost-effective and time-saving sequencing of the whole exome.

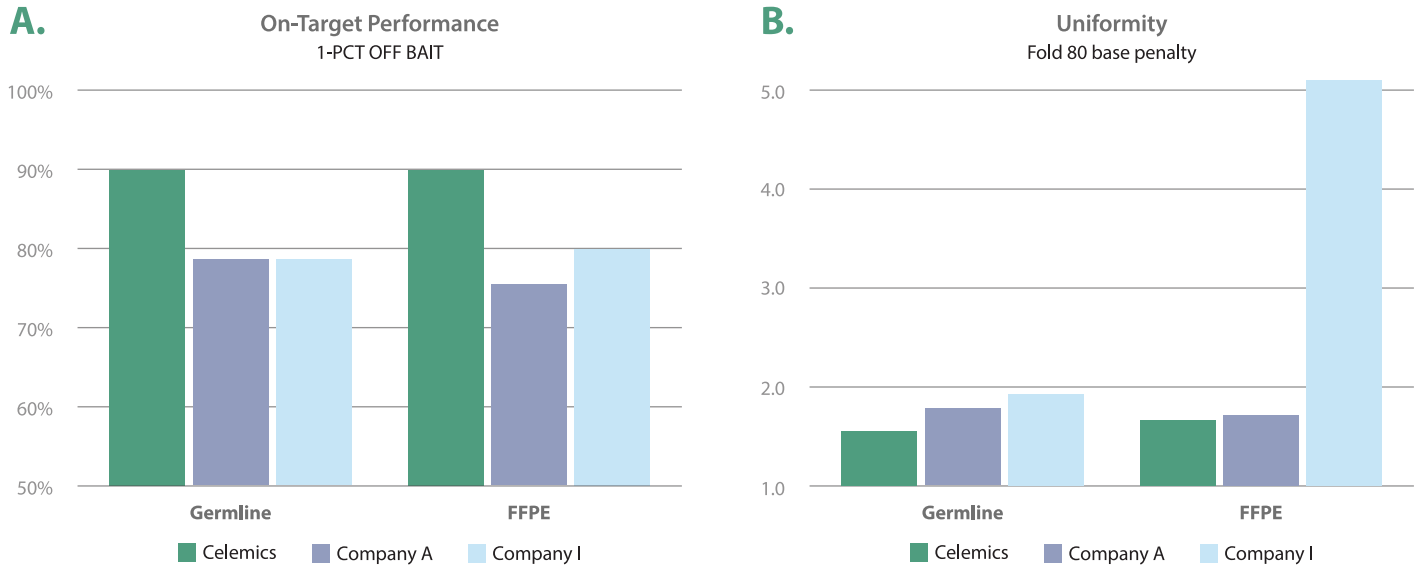

Figure 4. Superior Performance in the Market

Celemics WES Panel shows exceptional performance compared to other competitor products in both germline and FFPE analysis, measured by (A) 1-PCT OFF BAIT (higher the better), (B) Fold 80 base penalty (lower the better). Third-party laboratories (Certified Service Providers) conducted a comparison study between the Celemics WES Panel, Company A and Company I panels. Reference materials NA12878, NA12891, NA12892 for germline analysis, and HD832 for FFPE analysis were used with same amount. Illumina instruments were used for the sequencing. The data from the three panels were downsampled to 5.4 Gb.

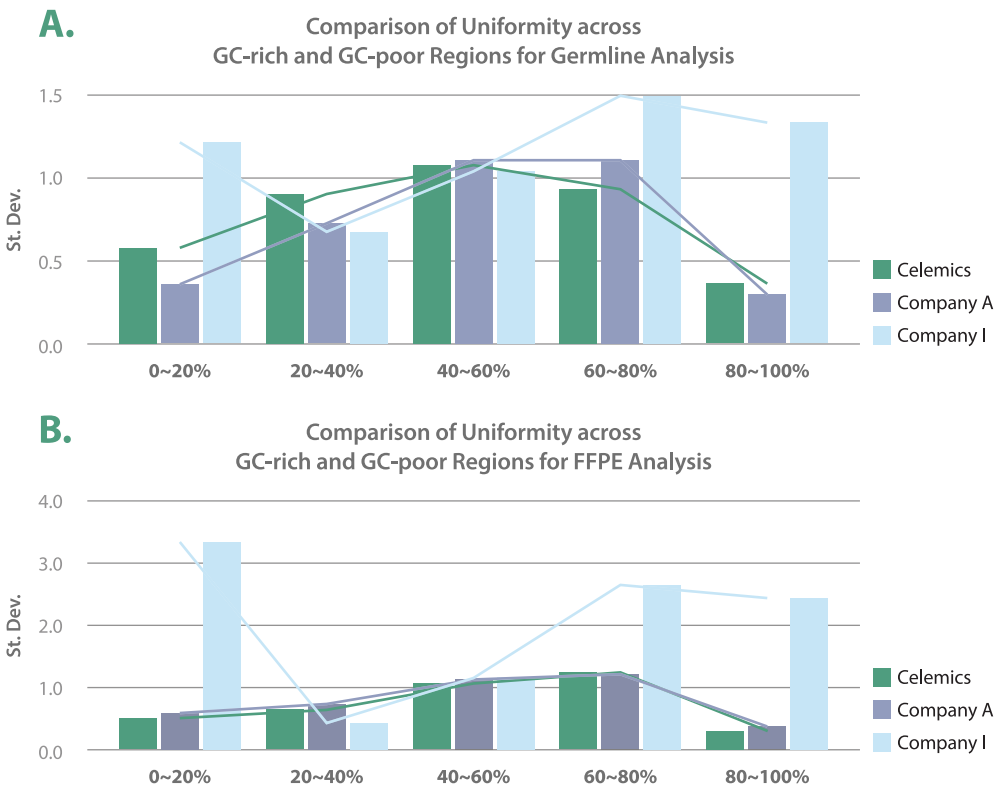

Figure 5. Exceptional Uniformity across Low and High GC Regions

(A) The Celemics WES Panel demonstrates minimal deviation, yielding 0.166 standard deviations (lower the better) across GC-rich and AT-rich regions in comparison to competitor products yielding 0.199 and 0.356 standard deviations. (B) The bar graphs shown in different GC ratios also illustrate the consistent uniformity of Celemics WES Panel in comparison to the competitor products.

Simple Gene Add-On Customization

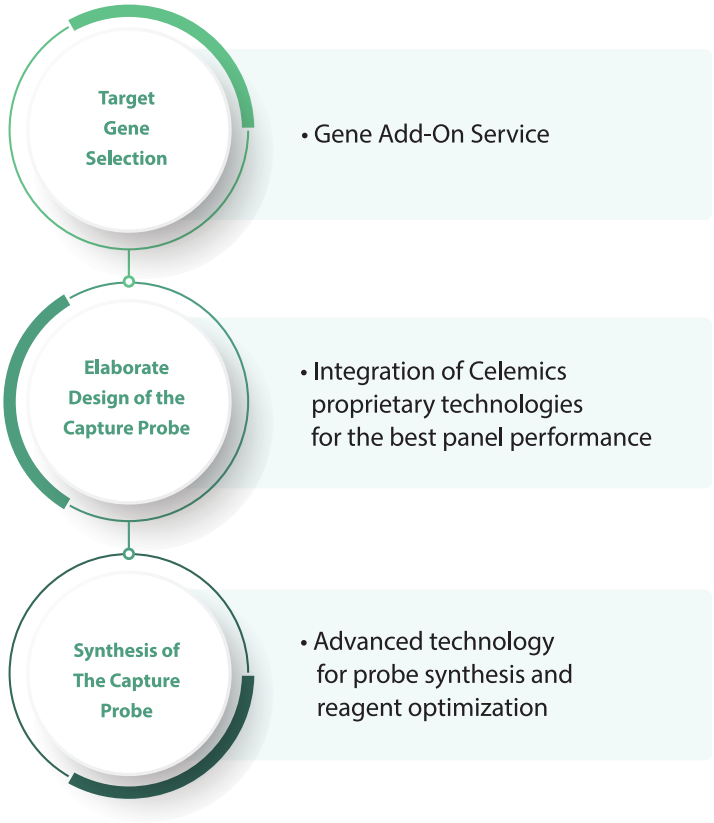

Figure 6. Flexible Customization with Gene Add-On Service

Celemics provides client-specific customization which is normally not available in the market. Most whole exome panels in the market are provided as a pre-set "ready-to-use" product and options for capturing the intronic or mitochondrial regions are often limited. Fortunately, Celemics is highly experienced with customized panels, allowing us to offer the Celemics WES bundled with a customizable Gene Add-On Service option. The addition of intronic regions or mitochondrial genomes to the WES panel enhances comprehensive assessment by capturing clinically significant genes embedded within those regions. The customized WES panel is provided with an option for evaluation through an in-house performance test for best quality results at an additional price.

Rapid Same-Day Workflow

Although hybridization capture has great advantages including minimized bias, stable and reliable data results from a variety of sample types, the complexity of the workflow and the long prep time have been obstacles to the users. Celemics has developed a new workflow and have incorporated it into our WES package to significantly simplify the process and reduce the experiment time. The conventional method took 2-3 days to complete one sequencing experiment. Now with Celemics' newly developed method, the whole experiment and the NGS run can be started on the same day.

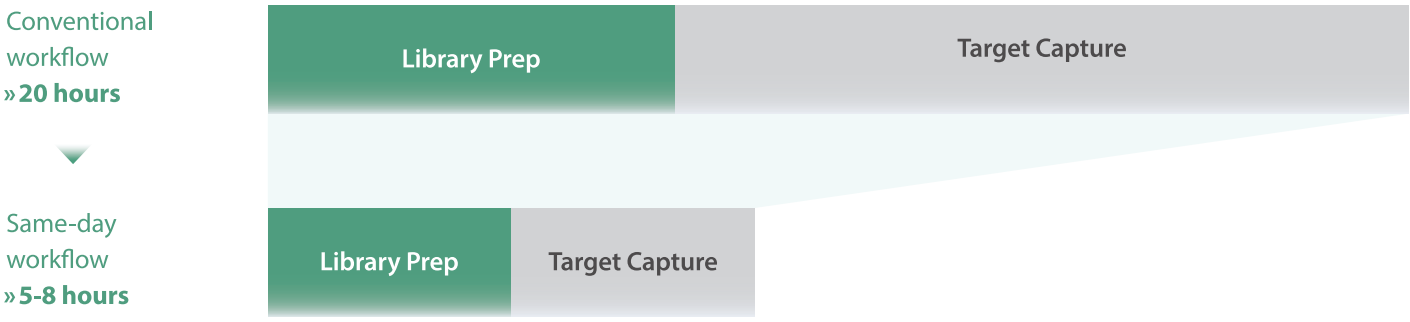

Figure 7. Newly Developed Same-Day Workflow

The figure demonstrates that Celemics has significantly reduced the time for performing Whole Exome Sequencing from the conventional 20 hours to 5 hour minimum workflow.

Full Bioinformatics Capability: FASTQ to Clinical Interpretation

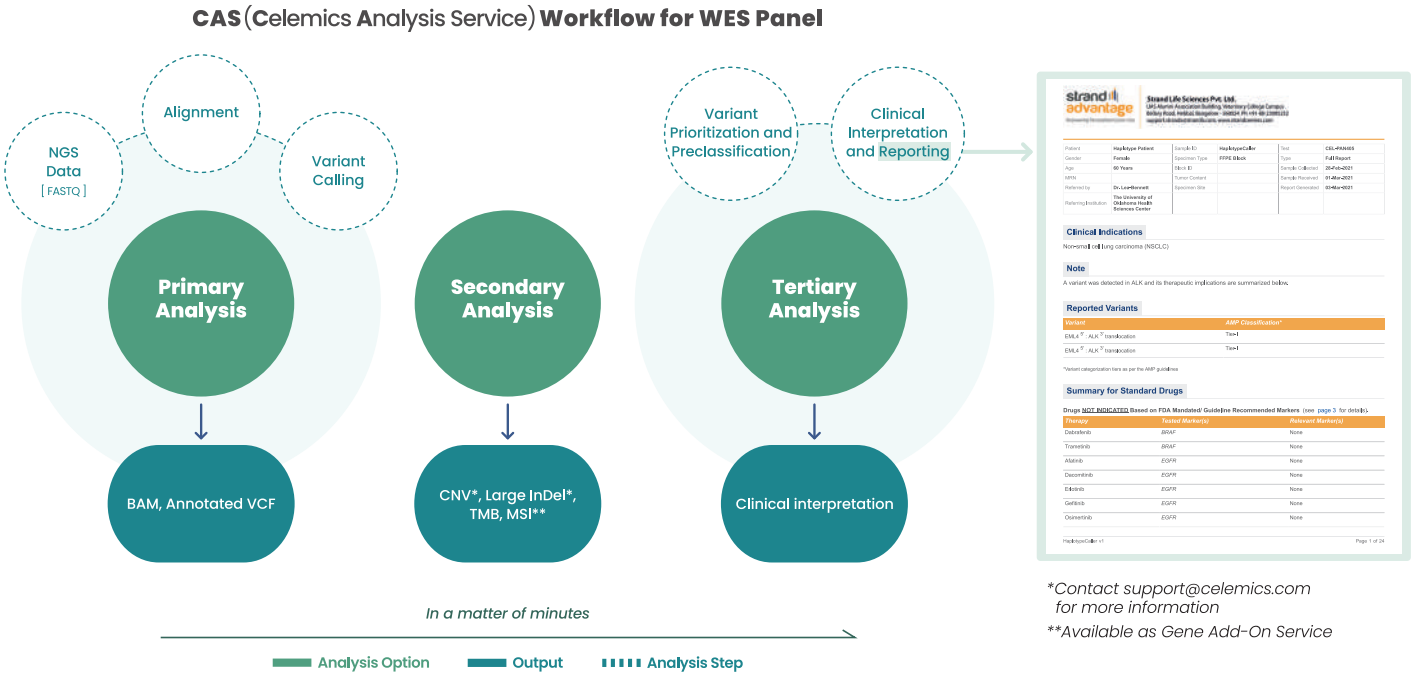

Figure 8. Bioinformatics Support through CAS

CAS (Celemics Analysis Service) provides easy data transmission by single-click and automated uploads. Due to the complete support from Celemics bioinformatics experts, CAS does not require separate third-party bioinformaticians. CAS also supports real-time troubleshooting throughout primary to tertiary analysis and client-specific customization.

strand advantage

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Patient	Haplotype Patient	Sample ID	HaplotypeCaller	Test	CEL-PAN405
Gender	Female	Specimen Type	FFPE Block	Type	Full Report
Age	60 Years	Block ID		Sample Collected	28-Feb-2021
MRN		Tumor Content		Sample Received	01-Mar-2021
Referred by	Dr. Lea-Bennett	Specimen Site		Report Generated	03-Mar-2021
Referring Institution	The University of Oklahoma Health Sciences Center				

Clinical Indications

Non-small cell lung carcinoma (NSCLC)

Note

A variant was detected in ALK and its therapeutic implications are summarized below.

Reported Variants

Variant	AMP Classification*
EML4 5' : ALK 3' translocation	Tier-I
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*Variant categorization tiers as per the AMP guidelines

Summary for Standard Drugs

Drugs NOT INDICATED Based on FDA Mandated/ Guideline Recommended Markers (see page 3 for details).

Therapy	Tested Marker(s)	Relevant Marker(s)
Dabrafenib	BRAF	None
Trametinib	BRAF	None
Afatinib	EGFR	None
Dacomitinib	EGFR	None
Erlotinib	EGFR	None
Gefitinib	EGFR	None
Osimertinib	EGFR	None

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Standard Drugs

Alectinib Enhanced Response

Markers

ALK

Evidence Details

Alectinib is a second generation ALK inhibitor approved for the treatment of patients with ALK-rearrangement positive non-small cell lung cancer (NSCLC). Alectinib has shown clinical benefit in both crizotinib pre-treated and treatment naive ALK positive NSCLC patients in multiple clinical studies [1,2], [3], [4], [5], [6]. The phase III ALEX study comparing response to alectinib and crizotinib in advanced ALK-positive NSCLC patients (n=303), found alectinib to be superior to crizotinib in terms of clinical benefit with a significantly higher 12-month event-free survival rate with alectinib (68.4% with alectinib vs. 48.7% with crizotinib), event of CNS progression in 18% of alectinib treated patients compared to 45% in the crizotinib treated group and a response rate of 82.9% in the alectinib group vs 75.5% in the crizotinib group [2].

Marker Details

EML4 (NM_019063, Exon 1-6) : ALK (NM_004304, Exon 20-29)
Oncogenicity Established by in-vitro Studies
EML4-ALK translocation is the most common aberration of the ALK gene, which is seen exclusively in lung cancer and represents 2-7% of the lung cancers cases [7]. The fusion gene results from an inversion event on the short arm of chromosome 2 and has constitutive ALK kinase activity [8]. Till date, over 11 EML4-ALK fusion variants have been identified in lung cancer, composed of varying EML4 transcript length fused with exon 20 of ALK [9].

EML4 (NM_001145076, Exon 1-5) : ALK (NM_004304, Exon 20-29)
Oncogenicity Established by in-vitro Studies
EML4-ALK translocation is the most common aberration of the ALK gene, which is seen exclusively in lung cancer and represents 2-7% of the lung cancers cases [7]. The fusion gene results from an inversion event on the short arm of chromosome 2 and has constitutive ALK kinase activity [8]. Till date, over 11 EML4-ALK fusion variants have been identified in lung cancer, composed of varying EML4 transcript length fused with exon 20 of ALK [9].

Drug Description

An orally available inhibitor of the receptor tyrosine kinase anaplastic lymphoma kinase (ALK) with antineoplastic activity. Upon administration, alectinib binds to and inhibits ALK kinase, ALK fusion proteins as well as the gatekeeper mutation ALKL1196M known as one of the mechanisms of acquired resistance to small-molecule kinase inhibitors. The inhibition leads to disruption of ALK-mediated signaling and eventually inhibits tumor cell growth in ALK-overexpressing tumor cells. ALK belongs to the insulin receptor superfamily and plays an important role in nervous system development. ALK dysregulation and gene rearrangements are associated with a series of tumors.
Source: The National Cancer Institute's Cancer Drug Information

References

1. Liao BC *et al.* 2015. Treating patients with ALK-positive non-small cell lung cancer: latest evidence and management strategy. *Ther Adv Med Oncol.* 7 (5):274-90 [PMID: 26327925].

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Figure 9. Clinical Interpretation Report

Celemics provides robust clinical interpretation services through a CAP-accredited partner that combines bioinformatics algorithms, public data from external sources/knowledge databases, visualization interfaces and reporting capabilities. The report includes pathogenicity and drug associated information.

No Need for Heavy Instruments

In order to perform Library Preparation prior to Target Enrichment and Sequencing, it is often required to have heavy instruments (such as a vacuum concentrator or sonicator, etc.), which are barriers against complete automation. Even with an automation protocol, using these heavy instruments is inevitable and is often burdensome to the users. Celemics has successfully eliminated the need for heavy instruments by substituting them with a more convenient solution of enzymes and beads. After rigorous validation that consistently showed reliable performance, we have optimized this workflow to enable the benefit of a complete walkaway solution.

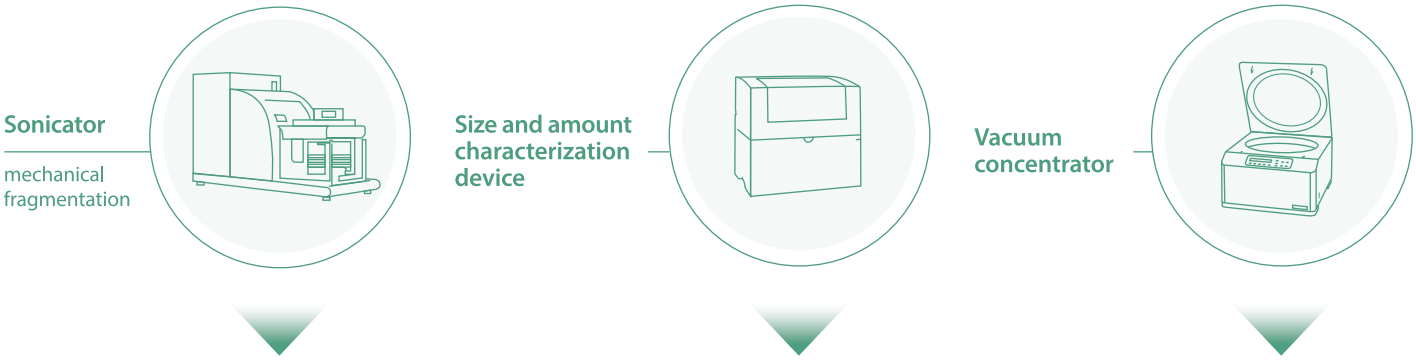

Figure 10. No Need for Heavy Instruments

Celemics has developed and optimized an enzymatic fragmentation, bead-based concentration, and normalization process, which eliminates the requirements for heavy instruments such as a sonicator (mechanical fragmentation), vacuum concentrator, size and amount characterization device, etc.

Flexible Integration with NGS Sequencers & Complete Walkaway Automation

Figure 11. Compatibility with NGS Sequencers and Automation

The Celemics WES Panel is seamlessly integrated with all NGS instruments from Illumina, MGI, and Ion Torrent. Since there are no heavy instruments required, the experiment can be carried out with complete automation.

Ordering Information

Product Sorting Category / Sub-category	Applied Platform	Package Option	Product Unit
Ready-to-use panels / Whole Exome Sequencing	Illumina, Ion Torrent, MGI	1) All-in-one Package 2) Standard Package 3) Target Enrichment Package	1) Reaction basis: 16, 48, 96 rxn 2) Sample basis: 16, 96, and more options *Pre-capture pooling options: 4, 8, 12

*Promotion: pre-capture pooling of 4 sample libraries

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