Mimix™ Myeloid Cancer Panel gDNA Reference Standard

IVD

For In Vitro Diagnostic Use

REF HD829-IVD Mimix™ Myeloid Cancer Panel gDNA Reference Standard

Intended Use

The Mimix™ Myeloid Cancer Panel gDNA reference standard is a cell line derived control material that contains 22 variants across 19 genes relevant to myeloid cancer. It is intended for qualitative and/or quantitative monitoring of next-generation sequencing (NGS) and droplet digital polymerase chain reaction (ddPCR) assays designed to detect somatic mutations in human gDNA samples for *in vitro* diagnostic use.

This control can be used to monitor NGS and ddPCR workflow, test performance, assay variation and helps identify increases in random or systematic errors. This product is for professional laboratory use only.

Summary and Explanation

NGS assays are widely adopted by researchers as well as clinical and diagnostic laboratories to analyze the genetic make-up of patient-derived samples, making it useful to gain insightful data on common or rare diseases[1]. Providing high-throughput data, NGS helps identify genetic differences in patients or any genetic changes introduced as certain diseases progress[2]. Similarly, digital PCR workflows, including ddPCR, are commonly used to enhance traditional PCR performance by allowing a significantly increased number of reactions to be performed and analyzed real time[3].

The Mimix™ Myeloid Cancer Panel gDNA Reference Standard enables direct analysis of patient-derived DNA samples against a wide range of cancer-related somatic mutations for fast and accurate results as part of diagnostic tests and scientific research. The product is designed to fit into NGS and ddPCR workflows to help accurately analyze patient-derived samples.

The Mimix™ Myeloid Cancer Panel gDNA Reference Standard is a gDNA reference standard derived from well-characterized cell lines, mimicking patient-derived gDNA samples. It includes 6 insertions/deletions (INDELs), which can help users to optimize their assay's performance when sequencing challenging structural variants. In particular, due to the importance of FLT3 internal tandem duplications (FLT3-ITDs), which are present in nearly 25% of patients with AML, Revvity has engineered a large novel 300 bp insertion into FLT3 – which we have termed the "ITD300" variant. This is a very desirable feature of this new product, as it represents the types of large insertions that may be encountered in real patient samples but are very difficult to source for assay validation and optimization purposes. The Mimix™ Myeloid Cancer Panel gDNA Reference Standard is designed with 15 mutations present at 5% allele frequency, to support the calculation of clinically relevant limit of detection of somatic workflows. In addition, the product contains 7 mutations at 10-70% allele frequency to support the validation of higher frequency germline workflows. This diversity allows for comprehensive assessment of assay performance and quantitative accuracy.

The Mimix™ Myeloid Cancer Panel gDNA Reference Standard is a multiplex standard covering the mutations on the following genes: ABL1, ASXL1, BCOR, CBL, DNMT3A, EZH2, FLT3, GATA1, GATA2, IDH1, IDH2, JAK2, KRAS NPM1, NRAS, RUNX1, SF3B1, TET2, TP53.

Principles of Operation

The Mimix™ Myeloid Cancer Panel gDNA Reference Standard contains genomic DNA stored in Tris-EDTA, isolated from well-characterized cell lines to mimic patient samples. No synthetic DNA is incorporated into this product. The gDNA is intended to be integrated into the customer's workflow for DNA extraction. Every batch of our Mimix™ Myeloid Cancer Panel gDNA has 22 variants confirmed by NGS and ddPCR (Table 1). This provides an accurate and reliable set for comparison to any NGS assay's performance.

In addition to ddPCR and NGS, further quality control of this product was performed via spectrophotometry.

Table 1: Verified variants by NGS and the corresponding allelic frequencies (AF) confirmed by ddPCR.

Gene	Variant (AA)	CDS mutation	GRCh38 co-ordinates	Expected AF by ddPCR	Acceptance range for ddPCR
ABL1	T315I	c.1001C>T	9:130872896	5.00%	4.00 – 6.00%
ASXL1	G646Wfs*12	c.1934dup	20:32434638	40.00%	36.00 – 44.00%
ASXL1	W796C	c.2388G>T	20:32435100	5.00%	4.00 – 6.00%
BCOR	Q1208Tfs*8	c.3621dup	X:40063833	70.00%	63.00 – 77.00%
CBL	S403F	c.1208C>T	11:119278278	5.00%	4.00 – 6.00%
DNMT3A	R882C	c.2644C>T	2:25234374	5.00%	4.00 – 6.00%
EZH2	R418Q	c.1253G>A	7:148817379	5.00%	4.00 – 6.00%
FLT3	D835Y	c.2503G>T	13:28018505	5.00%	4.00 – 6.00%
FLT3	ITD300	N/A*	13:28033909	5.00%	4.00 – 6.00%
GATA1	Q119*	c.355C>T	X:48791978	11.00%	10.00 – 12.00%
GATA2	G200Vfs*18	c.599del	3:128485998	35.00%	31.50 – 38.50%
IDH1	R132C	c.394C>T	2:208248389	5.00%	4.00 - 6.00%
IDH2	R172K	c.515G>A	15:90088606	5.00%	4.00 - 6.00%
JAK2	F537-K539>L	c.1611_1616del	9:5070021	5.00%	4.00 - 6.00%
JAK2	V617F	c.1849G>T	9:5073770	5.00%	4.00 - 6.00%
KRAS	G13D	c.38G>A	12:25245347	40.00%	36.00 – 44.00%
NPM1	W288Cfs*12	c.860_863dup	5:171410539	5.00%	4.00 – 6.00%
NRAS	Q61L	c.182A>T	1:114713908	10.00%	9.00 – 11.00%
RUNX1	M267I	c.801G>A	21:34834414	35.00%	31.50 – 38.50%
SF3B1	G740E	c.2219G>A	2:197401989	5.00%	4.00 – 6.00%
TET2	R1261H	c.3782G>A	4:105243757	5.00%	4.00 – 6.00%
TP53	S241F	c.722C>T	17:7674241	5.00%	4.00 – 6.00%

*- Variant type not called by variant caller (large insertion, CN variant, fusion, indel).

Material Provided: Reagents

Mimix™ Myeloid Cancer Panel gDNA Reference Standard

- Catalogue/Model number: HD829-IVD
  One vial, 1x 20µL
  Material provided in Tris-EDTA (10 mM Tris-HCl, 1 mM EDTA), pH 8.0.

⚠ Precautions and Warning

- Although this product is not classified as dangerous, handle all materials as potentially biohazardous, following standard laboratory safety procedures.
- Dispose of all waste materials in accordance with local regulations.
- Inspect the vial for any signs of damage or leakage.

Storage and Handling

- Store unopened at 2 to 8 °C.
- Centrifuge briefly before opening and make sure all contents are at the bottom of the tube.
- Do not use this product beyond the expiration date printed on the product label.

Interpretation of Results

Variant detection results for the Mimix™ Myeloid Cancer Panel gDNA may vary depending on the library preparation method, sequencing platform, and bioinformatics pipeline used for NGS assays, as well as primer/probe set, analysis type/platform, and assay conditions for ddPCR. The expected variant list of the Mimix™ Myeloid Cancer Panel gDNA provided can be used to compare each subsequent run.

Quality Control and Performance Characteristics

Following our QC procedure, our acceptance criteria are described below (Table 2). Users should note that results will vary depending on the equipment and workflow used. Users are expected to perform their own validation to determine AFs within the workflow to be monitored. The below reported results were obtained using the validated equipment and workflow specified for each assay.

Table 2. List of quality control tests applied and the corresponding acceptance criteria.

Test name	Test purpose	Acceptance criteria
Spectro-photometry	Measure quality and quantity of gDNA	Concentration: 24.00-26.00 ng/µL (260/280 ratio): 1.75 – 2.00
ddPCR	Measure AF	Varies per gene. See Table1.

The gDNA yields and purity obtained from different batches of the Mimix™ Myeloid Cancer Panel gDNA Reference Standard are shown in Figures 1 and 2 respectively. ddPCR results showing allelic frequencies across Mimix™ Myeloid Cancer Panel gDNA Reference Standard batches are presented in Figure 3.

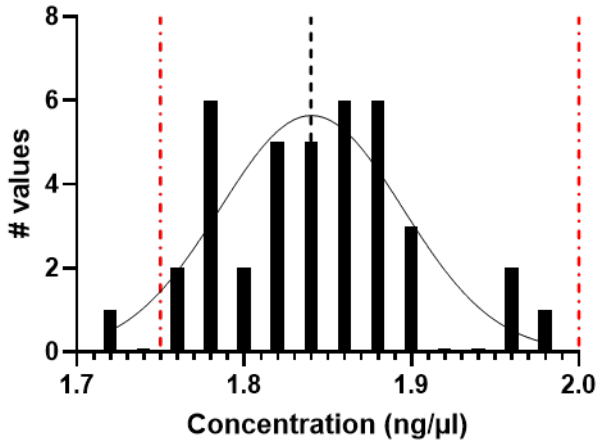

Figure 1. Concentration of product batches measured by spectrophotometry. The data shows the frequency distribution of each datapoint. The graph displays the mean concentration (black dotted line) and limits of the acceptance criteria (red dotted lines).

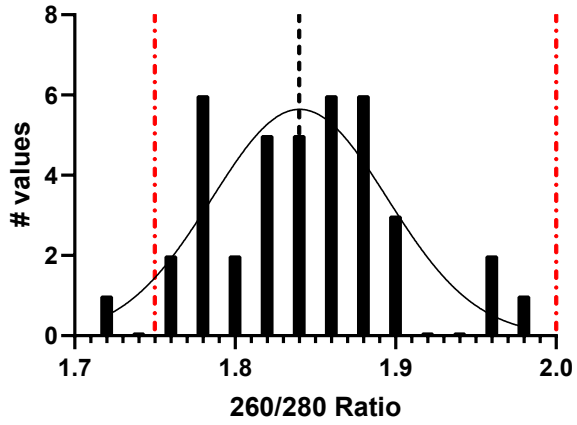

Figure 2. Frequency distribution histogram showing the purity of Mimix™ Myeloid Cancer Panel. The mean 260/280 ratio is indicated by a dotted black line with the upper and lower limits of the acceptance criteria indicated by red dotted lines.

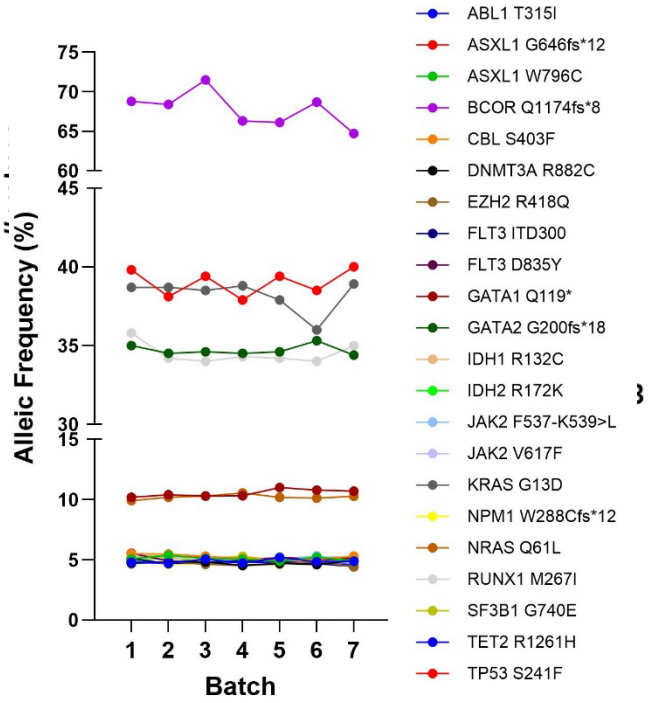

Figure 3. Allelic frequencies measured by ddPCR in separate Mimix™ Myeloid Cancer Panel gDNA Reference Standard batches.

Limitations

- The Mimix™ Myeloid Cancer Panel gDNA Reference Standard is not to be used as a substitute for the internal controls provided by manufacturers within their IVD assay kits.

Technical Support

Scientific support
Tel: 800-235-9880 (Option 2) Or 303-604-9499 (Option 2)
Fax: 1-800-292-6088 Or 303-604-9680
Email: technical@horizondiscovery.com

Customer support
Tel: 800-235-9880 (Option 1) Or 303-604-9499 (Option 1)
Fax: 1-800-292-6088 Or 303-604-9680
Email: orders@horizondiscovery.com

For a high-confidence variant list go to https://horizondiscovery.com/reference-standards/products/myeloid-cancer-panel-gdna-reference-standard-ivd

Batch-specific whole exome sequencing data is provided upon purchase as an online link.

References

1 Vinkšel, M., Writzl, K., Maver, A. *et al*. Improving diagnostics of rare genetic diseases with NGS approaches. *J Community Genet* 12, 247–256 (2021). https://doi.org/10.1007/s12687-020-00500-5

2 Boycott K, Hartley T, Adam S, et al. The clinical application of genome-wide sequencing for monogenic diseases in Canada: Position Statement of the Canadian College of Medical Geneticists. *J Med Genet*. 2015;52(7):431-437. doi:10.1136/jmedgenet-2015-103144

3 Mirabile A, Sangiorgio G, Bonacci PG, et al. Advancing Pathogen Identification: The Role of Digital PCR in Enhancing Diagnostic Power in Different Settings. *Diagnostics (Basel)*. 2024;14(15):1598. Published 2024 Jul 25. doi:10.3390/diagnostics14151598

Glossary

IVD In Vitro Diagnostic Medical Device

REF Catalogue Number

Legal Manufacturer

Temperature Limit

Caution

NON STERILE Non-sterile

Consult Instructions for Use

Use-by date

UDI Unique device identifier

QTY Quantity

CONTROL + Positive control

Trademark and Patent information

Horizon Discovery Biosciences Limited is a wholly owned subsidiary of Revvity Discovery Limited. Revvity Discovery Limited and Horizon Discovery Biosciences Limited are indirectly wholly owned subsidiaries of Revvity, Inc.

Mimix is a trademark of Revvity Health Sciences Inc.

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Document ID: 03-09-206
Version: 00

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