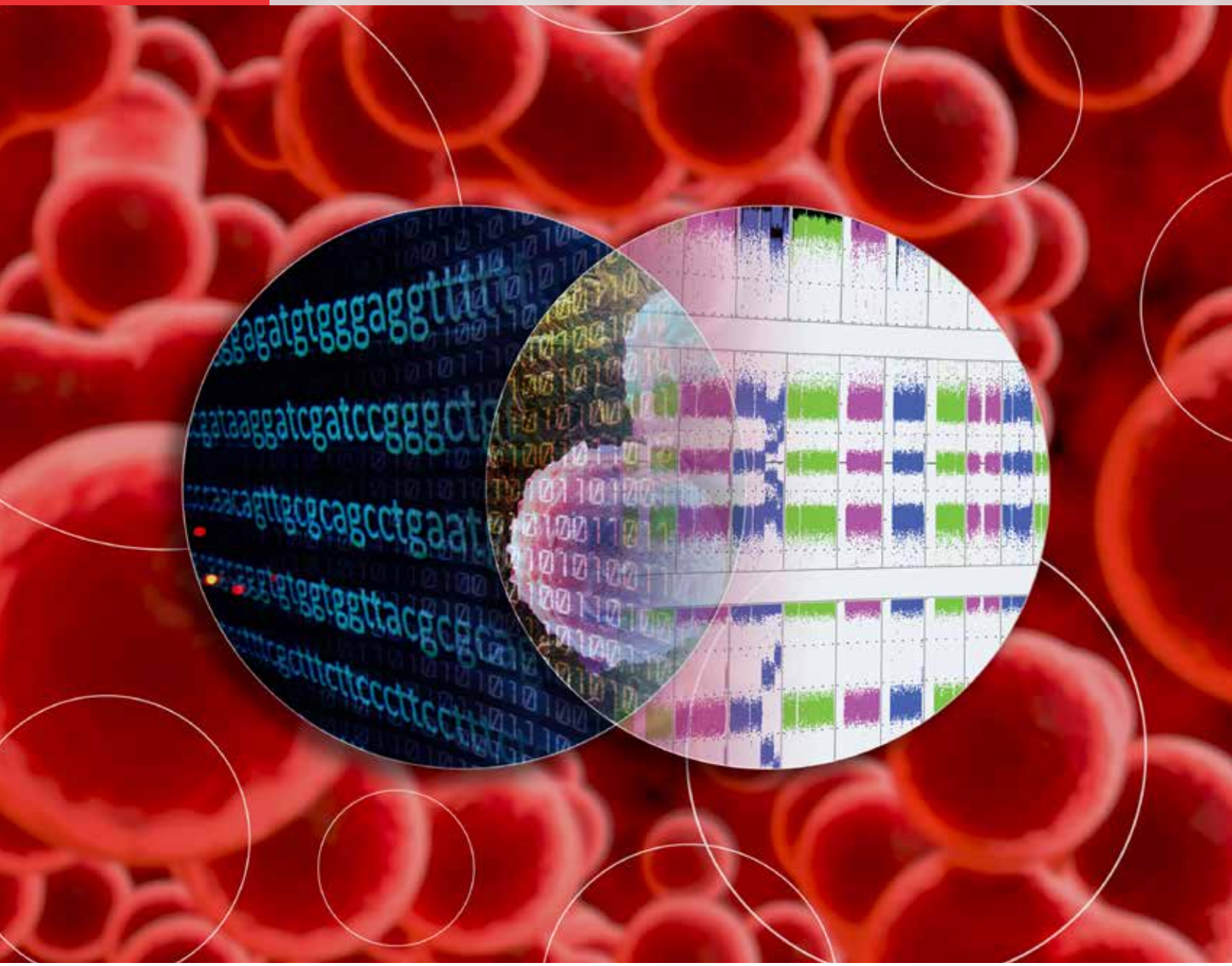


Simplifying hematological malignancy profiling

Delivering faster answers through the combined power of just two platforms

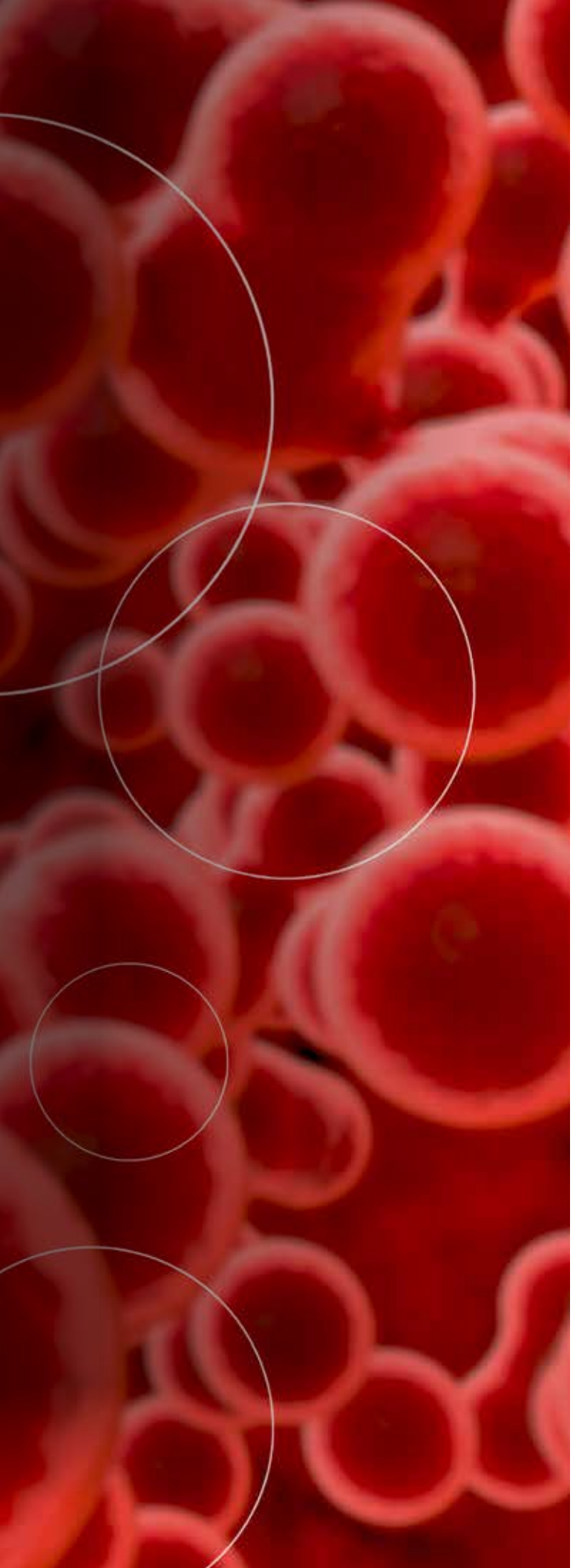
ThermoFisher SCIENTIFIC

Simplifying hematological malignancy profiling

Hematological malignancies are known to have a multitude of aberrations across the genome, including somatic mutations, fusion genes, and copy number alterations (CNAs) such as duplications, deletions, loss of heterozygosity (LOH), copy neutral LOH (cnLOH), changes in ploidy, and more. Yet no one technology can efficiently assess all of these aberration types, making the profiling of hematological malignancies time- and labor-intensive.

Using our technologies, you no longer need four or more separate tools for comprehensive molecular profiling of your hematological malignancy samples. Our proven microarray and next-generation sequencing (NGS) technologies—together with combined reporting—provide a more comprehensive, cost-effective, and streamlined solution for hematological malignancy sample analysis.

Techniques	Results
FISH, qPCR, Sanger sequencing, and karyotyping	• Well-established technologies, but may miss important information due to lack of coverage • Costly and time-consuming to perform four or more techniques • Matching different reports from the different technologies is time-intensive and challenging
Microarray analysis and NGS	• More comprehensive profiling, so important aberrations are not missed • Cost-effective and more streamlined solution for faster results • Straightforward analysis with a single, integrated report for both microarray and NGS results



Contents

Hematological malignancy driver events—somatic mutations, fusions and CNAs

Background: the importance of comprehensive genomic analysis

While fusion genes are known as important drivers of certain hematological malignancies [1], additional studies have also identified cancers characterized by recurrent copy number changes (C class) and recurrent mutations (M class), highlighting the importance of comprehensive genomic analysis of hematological cancer samples.

C class cancers

Many reports have reviewed the importance of CNAs as major cancer drivers in hematological malignancies [2-4]. These findings have also shown that genome-wide CNAs are the most informative somatic events for potential future prognostic and predictive markers.

For these C class hematological cancers, assays for somatic copy number alterations are ideal to assess the quantity of a gene, looking for any deviations from a constitutional state [5].

M class cancers

While numerous hematological malignancies are phenotypically similar, they often have characteristic somatic mutations in many genes, allowing them to be classified according to their gene mutation profile [6-7]. These gene mutation profiles can provide potential diagnostic, prognostic, and therapeutic information.

In these M class hematological cancers, assays for somatic mutations are ideal to assess the quality of a gene, looking for any mistake in the DNA sequence.

Simple yet comprehensive hematological malignancy sample profiling

Whole-genome microarray with targeted NGS—a powerful pairing for hematological cancer research

Technique	Application	Importance
Whole-genome microarray	Identify whole-genome copy number changes	• Increases the detection of abnormalities as compared to karyotyping, FISH, SNP arrays, and array CGH • Able to identify new abnormalities • Able to process one to tens of samples per day
	Detect copy number gains and losses, LOH, cnLOH, ploidy changes, mosaicism, and clonal heterogeneity in a single assay	• Obtain the most information from a single sample • Accurately profile copy number variations in hematological malignancies
	Relevant cancer types: ALL, CLL, and MDS as well as emerging evidence for AML, CML, and MM	
Targeted NGS	Screen and identify cancer-specific somatic mutations such as single-nucleotide variants (SNVs), insertions or deletions (indels), and gene fusions	• Obtain a comprehensive view of DNA mutations (SNVs and indels) together with all major gene fusion transcripts for myeloid malignancies • Analyze and detect even challenging genes like *CEBPA* and the internal tandem duplications of *FLT3* (*FLT3*-ITDs) • Consolidate complex workflows into one end-to-end solution and save resources for verification and QC
	Interrogate all myeloid disorders and associated genetic abnormalities in a single test run (1–12 samples/chip)	• Obtain the most information from a single sample • Easily assess samples from multiple disorders in a single run, saving time and resources
	Relevant cancer types: AML, CML, CMML, JMML, MDS, and MPN	

CytoScan HD Suite

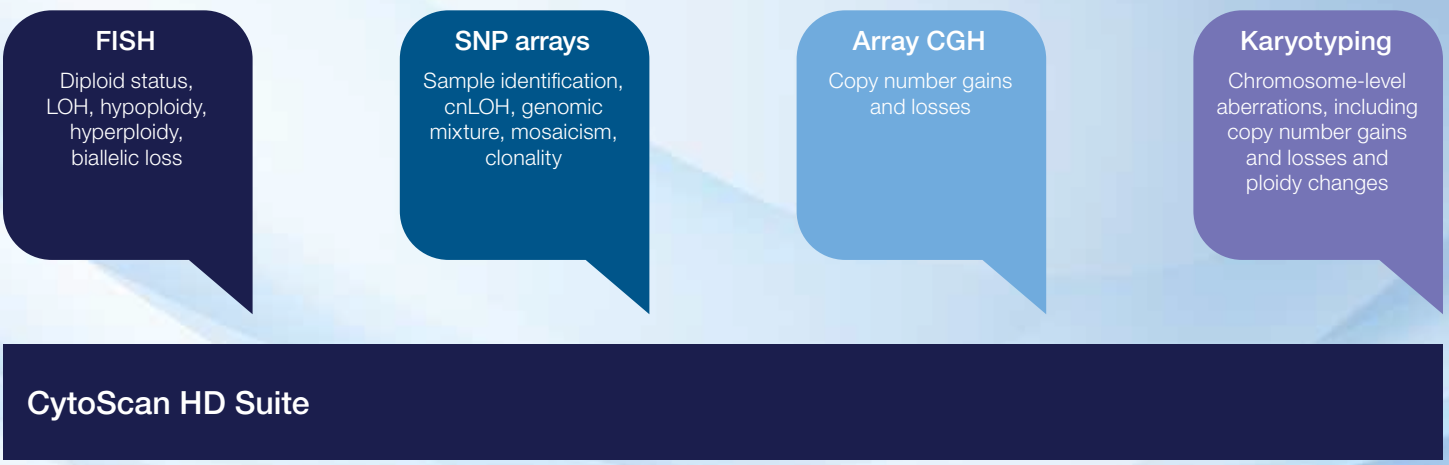
See more copy number changes with microarray analysis

The Applied Biosystems™ CytoScan™ HD Suite is used in labs worldwide to interpret complex karyotypes, delivering very high resolution so you do not miss important aberrations. Comprising arrays, reagents, and free data analysis software, the CytoScan HD Suite offers:

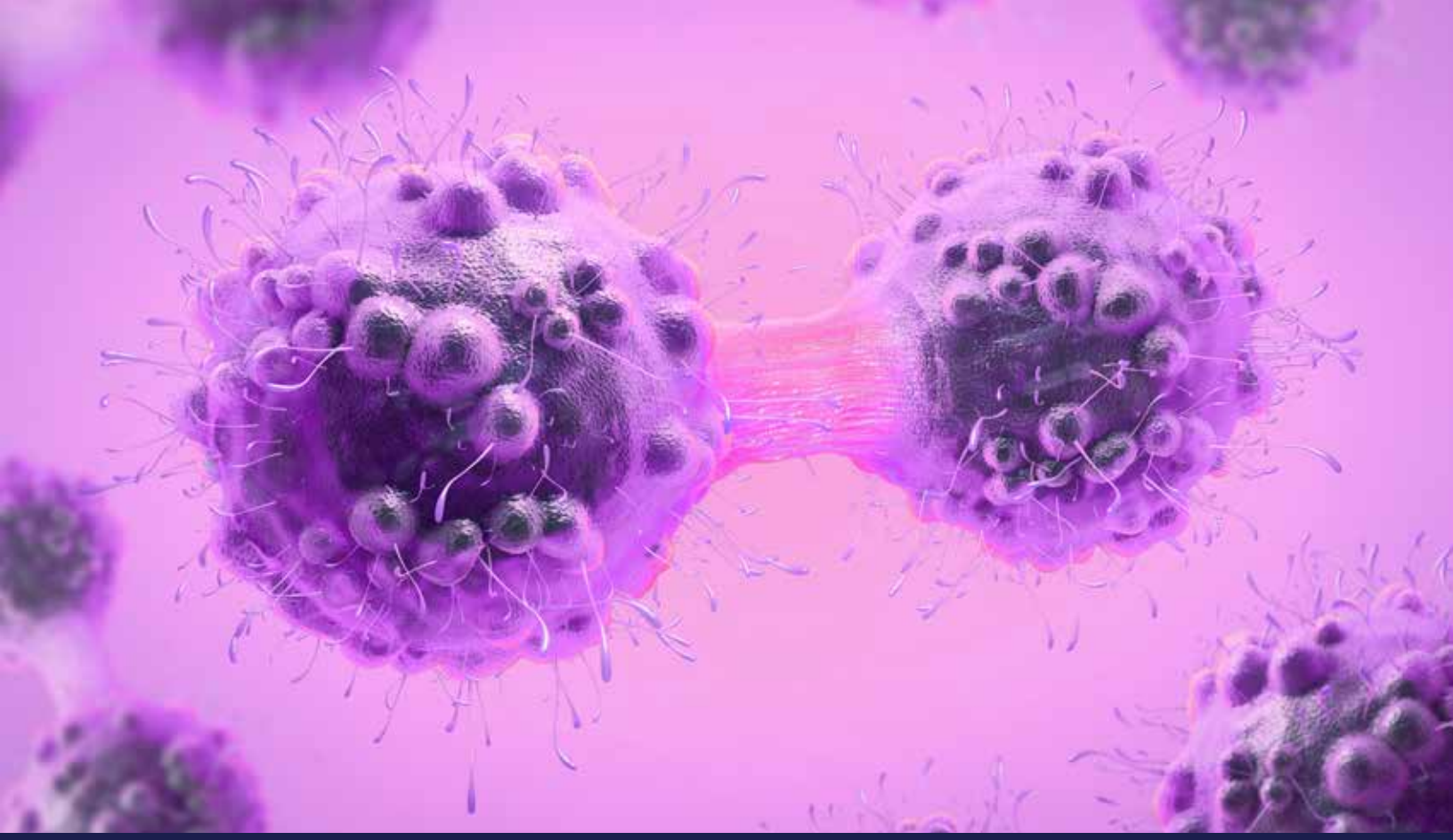
- **Comprehensive coverage**—providing whole-genome analysis of genes with established significance as well as those with emerging evidence, thus helping to eliminate future revalidation burden
- **High detection sensitivity**—elucidating patterns of clonal diversity, heterogeneous samples, and structural inconsistencies in low-level mosaics
- **An all-in-one assay**—detecting chromosomal arm aberrations, focal changes, LOH, and cnLOH, and obtaining sample identification with a single assay, reducing cost and processing time
- **Fast turnaround time**—enabling sample to answer (with sample prep automation on the Applied Biosystems™ NIMBUS™ Target Preparation Instrument), including data analysis, in just 3 days

"The genetic complexity of cancer cells in hematological malignancies requires a comprehensive approach for detection of relevant changes. The identification of copy number gains and losses, LOH, cnLOH, clonal heterogeneity, and ploidy status as well as mosaicism are all critical for evaluating blood cancer samples to discover new biomarkers. The CytoScan HD assay has enabled us to accurately analyze many aberrations in blood cancer samples."

Dr. Alka Chaubey
Greenwood Genetic Center



CytoScan HD Suite provides data otherwise only obtained from four separate technologies.



"We're searching for new biomarkers in hematological malignancies with potential diagnostic, prognostic, or predictive value. Microarrays play a large role in the process of identifying new genomic signatures in a fast and cost-effective manner. The protocols for data analysis are well established, making microarrays a useful platform for whole-genome copy number profiling in hematological malignancies."

Dr. Claude Preudhomme
Centre Hospitalier Régional Universitaire de Lille

Simple data analysis and reporting

Applied Biosystems™ Chromosome Analysis Suite (ChAS) is simple yet powerful analysis software that enables you to view and summarize genome-wide chromosomal aberration data from the CytoScan HD Suite with just a few clicks. Streamlined reporting through Ion Torrent™ Oncomine™ Knowledgebase Reporter allows you to more easily transform your data into decisions.

Visualize your results your way	Quickly obtain calls and annotations	Directly access multiple databases	Interpret results with integrated reporting
• Chromosome view • Copy number and LOH view	• Easily identify and annotate changes for fast interpretation	• NCBI • UCSC • Genome Browser • Ensembl • BED/AED • OMIM	• Link variants to labels, guidelines, and clinical trials

Oncomine Myeloid Research Assay

The power of NGS for somatic mutation and gene fusion analysis

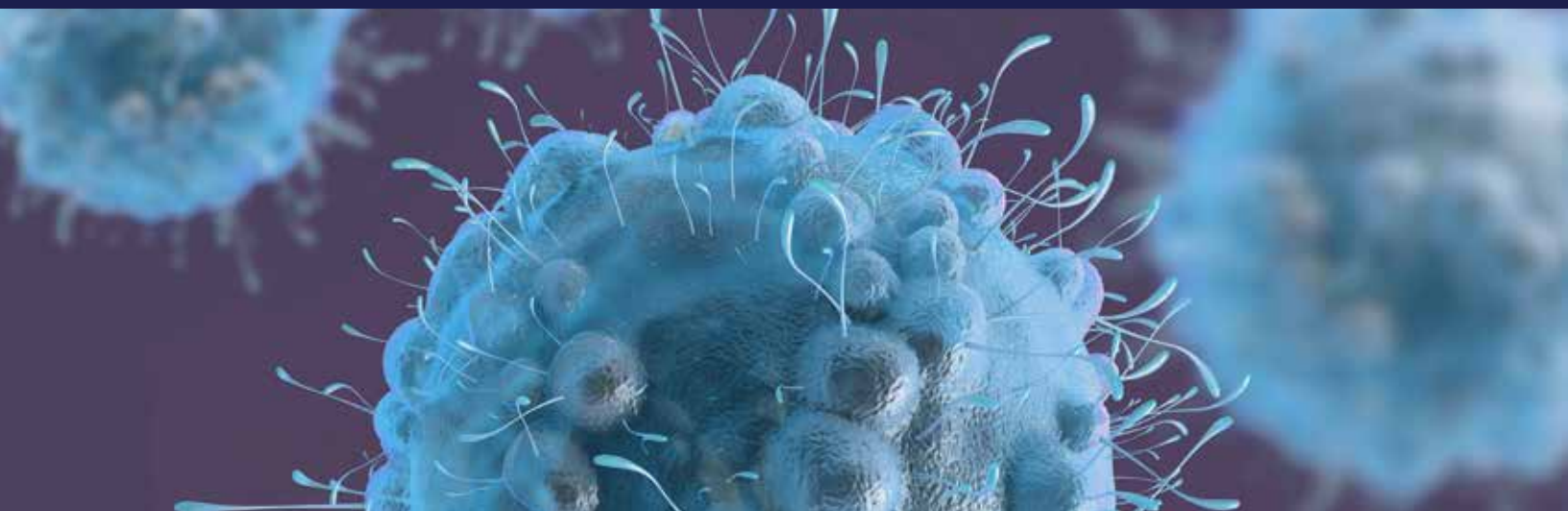
The Ion Torrent™ Oncomine™ Myeloid Research Assay enables profiling of multiple relevant driver genes from all major myeloid disorders in a single test, significantly consolidating the classic molecular analysis protocol, decreasing turnaround time, and potentially increasing diagnostic yield. This assay is compatible with both the Ion PGM™ and Ion GeneStudio™ S5 series systems and comes with either manual or automated library preparation configurations for the Ion Chef™ System. It also includes clear analysis and reporting, providing an end-to-end workflow that is optimized for oncology research.

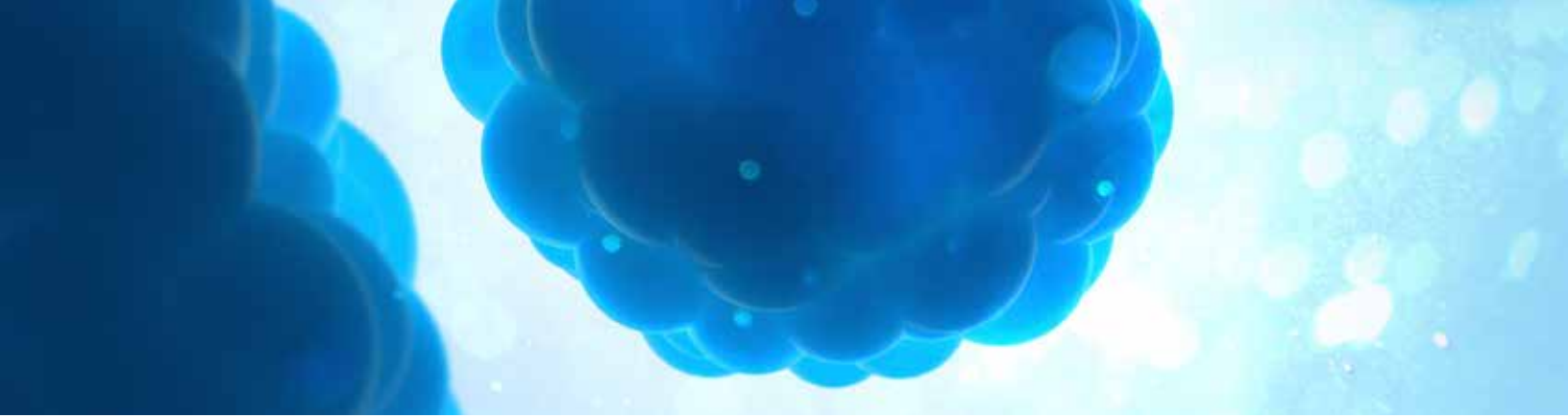
The Oncomine Myeloid Research Assay offers:

- **Ease of use**—DNA variants and RNA variants can be profiled using one assay with automated library preparation
- **Effective design**—great coverage of challenging targets such as *CEBPA* and *FLT3*-ITDs
- **Flexibility**—verified with blood and bone marrow samples on the Ion PGM and Ion GeneStudio S5 systems with manual and automated library preparation
- **Speed**—from samples to answers in just 2–3 days with up to 4 samples on the Ion 318™ Chip or 12 samples on the Ion 530™ Chip

"With the Ion Torrent myeloid panel, we could move the testing of all myeloid malignancies to one assay and improve on turnaround time while keeping the cost down. In our assessment of previously characterized samples, we had excellent concordance for relevant variants, including fusions."

Dr. Nancy Carson
Saint John Regional Hospital





Comprehensive coverage

The Oncomine Myeloid Research Assay comprises 40 key DNA target genes and 29 driver genes in a broad fusion panel to cover all the major myeloid disorders.

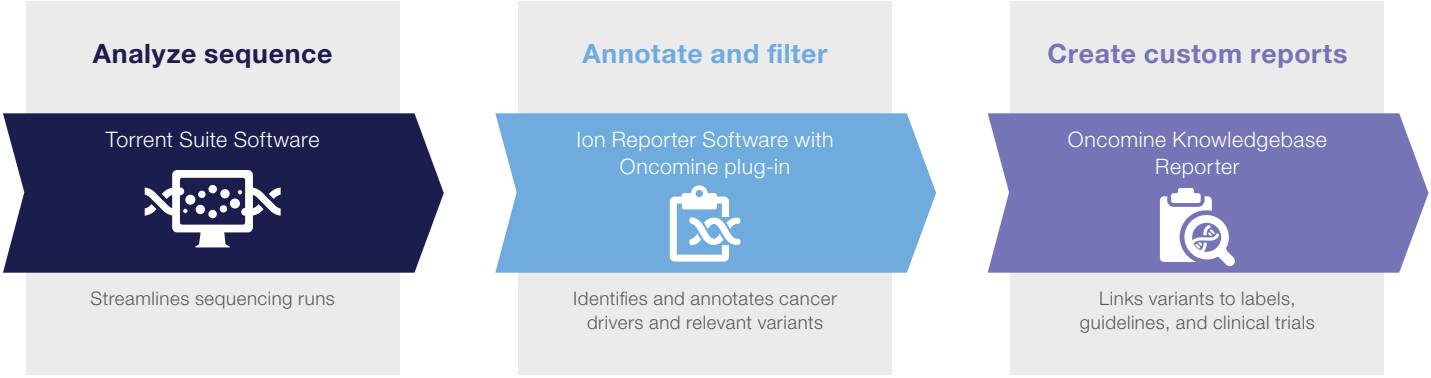
Oncomine Myeloid Research Assay target genes.

Hotspot genes (23)		Full genes (17)		Fusion driver genes (29)			Expression genes (5)	Expression control genes (5)
ABL1	*KRAS*	*ASXL1*	*PRPF8*	*ABL1*	*HMGA2*	*NUP214*	*BAALC*	*EIF2B1*
BRAF	*MPL*	*BCOR*	*RB1*	*ALK*	*JAK2*	*PDGFRA*	*MECOM*	*FBXW2*
CBL	*MYD88*	*CALR*	*RUNX1*	*BCL2*	*KMT2A*	*PDGFRB*	*MYC*	*PSMB2*
CSF3R	*NPM1*	*CEBPA*	*SH2B3*	*BRAF*	*(MLL)*	*RARA*	*SMC1A*	*PUM1*
DNMT3A	*NRAS*	*ETV6*	*STAG2*	*CCND1*	*MECOM*	*RBM15*	*WT1*	*TRIM27*
FLT3	*PTPN11*	*EZH2*	*TET2*	*CREBBP*	*MET*	*RUNX1*		
GATA2	*SETBP1*	*IKZF1*	*TP53*	*EGFR*	*MLLT10*	*TCF3*		
HRAS	*SF3B1*	*NF1*	*ZRSR2*	*ETV6*	*MLLT3*	*TFE3*		
IDH1	*SRSF2*	*PHF6*		*FGFR1*	*MYBL1*			
IDH2	*U2AF1*			*FGFR2*	*MYH11*			
JAK2	*WT1*			*FUS*	*NTRK3*			
KIT								

Streamlined informatics and reporting solution

Managing and ultimately interpreting the significant quantities of variant data produced by NGS present a formidable challenge for accurate and thorough but efficient and fast analysis of cancer-relevant data.

The Oncomine informatics workflow presents a sample-to-report data analysis solution—from initial sequence analysis of hundreds of variants to filtering down to relevant cancer drivers and creating a clear, uncluttered, and customizable report. This report can enhance your results by putting them into context with current knowledge and use in clinical oncology research, including on-market oncology labels, guidelines, and current global clinical trials.



A single report for microarray and NGS results

Simple, customizable analysis and reporting

The wide range of variants in cancer samples and the required use of multiple reports can present challenges for efficient, accurate, and thorough analysis of cancer-relevant data.

The Oncomine Knowledgebase Reporter helps you summarize the relevant cancer driver variants in a clear and simple report that links sample-specific variants to labels, guidelines, and current global clinical trials. It also enables integrated reporting with cytogenetic data from the CytoScan HD Suite and NGS data from the Oncomine Myeloid Research Assay.

With the Oncomine Knowledgebase Reporter, you can:

- Obtain a single report with results from both the CytoScan HD Suite and the Oncomine Myeloid Research Assay
- View relevant labels and guidelines for each variant
- Match your sample with local clinical trials
- Customize your report with flexible templates in 11 languages

The Oncomine Knowledgebase Reporter supports cytogenetic data with integrated reporting for myeloid cancers. Simply upload data from chromosomal alterations as reported by the CytoScan HD Suite to create custom reports with data and images.

Services and support

Providing fast responses by experienced scientists

More than 1,300 service and support specialists worldwide partner with you to help enable your scientific success through:

Service plans—planned maintenance and guaranteed response times to help you avoid unnecessary downtime, reduce strain on laboratory staff, and extend the life of your instruments

Compliance services—timely, cost-effective, and audit-ready documentation managed by a compliance specialist to help ensure your instrument is installed, operating, and performing to the manufacturer's specifications

Analytical validation (AV) consulting services—technical project management, data analysis support, and documentation of your lab's AV are provided to help develop and optimize your assay validation workflow for required parameters

Bioinformatics and IT services—optional consulting services with a bioinformatics application scientist to review software, applications, workflow optimization, and data management

Education services—application and instrument training programs are available at our training centers located throughout the world, within your lab, or through web-based instruction

Find out more about our services and support at
thermofisher.com/instrumentservices

Ordering information

Product	Description	Cat. No.
CytoScan HD Array Kit and Reagent Kit Bundle	Arrays and reagents for 24 assays	901835
CytoScan HD Kit Plus 24	Arrays and reagents for 24 assays plus *Taq* polymerase for 96 assays	905824
CytoScan HD Kit Plus 96	Arrays and reagents for 96 assays plus *Taq* polymerase for 96 assays	905896
Oncomine Myeloid Research Assay	Manual library preparation version—24 reactions	A36940
Oncomine Myeloid Research Assay—Chef Ready	Automated library preparation version—32 reactions	A36941

References

1. Watson IR, Takahashi K, Futreal PA et al. (2013) Emerging patterns of somatic mutations in cancer. *Nat Rev Genet* 14(10):703–718.
2. Kim TM, Xi R, Luquette LJ et al. (2013) Functional genomic analysis of chromosomal aberrations in a compendium of 8000 cancer genomes. *Genome Res* 23(2):217–227.
3. Zack TI, Schumacher SE, Carter SL et al. (2013) Pan-cancer patterns of somatic copy number alteration. *Nat Genet* 45(10):1134–1140.
4. Shlien A, Malkin D (2009) Copy number variations and cancer. *Genome Med* 1(6):62.
5. Baughn LB, Biegel JA, South ST et al. (2015) Integration of cytogenomic data for furthering the characterization of pediatric B-cell acute lymphoblastic leukemia: a multi-institution multi-platform microarray study. *Cancer Genet* 208(1–2):1–18.
6. Papaemmanuil E, Gerstung M, Bullinger L et al. (2016) Genomic classification and prognosis in acute myeloid leukemia. *N Engl J Med* 374(23):2209–2221.
7. The Cancer Genome Atlas Research Network (2013) Genomic and epigenomic landscapes of adult de novo acute myeloid leukemia. *N Engl J Med* 368(22):2059–2074.

Find out more about our hematological malignancy solutions at **thermofisher.com/hemeonc**

ThermoFisher SCIENTIFIC