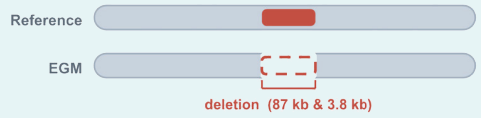
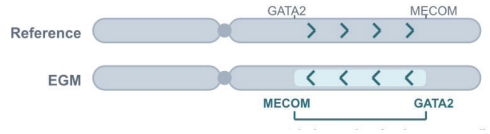
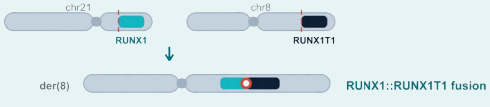
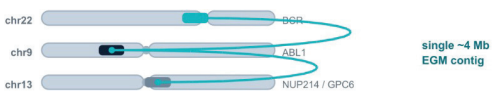
Bring Key Heme-Relevant Variants Into Focus

Discover Integrated Insights in One Workflow with the OhmX™ Platform

Current workflows for AML, MDS, and related hematological malignancies rely on a combination of technologies, each contributing different information. Integrating findings across multiple reports adds complexity, and critical variant classes remain difficult to resolve.

Electronic genome mapping (EGM) on the OhmX™ Platform is being developed to provide integrated analysis of disease-associated structural variants (SVs) and genome-wide copy number variants (CNVs) from a single whole-genome workflow. The representative examples shown highlight ongoing development across multiple heme-relevant SV classes, including insertions, deletions, inversions, translocations, complex rearrangements, and genome-wide CNVs.

Variant Class Overview

Variant Class	What EGM Resolves	Limitation of Current Methods
Insertion ***KMT2A*-PTD** 22 kb tandem duplication		Not detectable by karyotyping, fluorescence in situ hybridization (FISH), or targeted next-generation sequencing (NGS)
Deletion ***TP53*** 17p deletion · 87 kb & 3.8 kb		Targeted FISH probes miss small deletions and atypical breakpoints
Inversion **inv(3)(q21q26)** *MECOM – GATA2* enhancer		FISH confirms the event; fusion partner and CNV context require separate assays
Translocation ***RUNX1::RUNX1T1*** t(8;21)		FISH identifies common fusions; full breakpoint architecture and allele-level resolution require additional testing
Complex rearrangement ***BCR::ABL1*** chr 9 · 13 · 22		Full three-chromosome architecture not resolved by any single standard cytogenetic method
Copy number variation **Genome-wide** Gains & losses		Chromosomal microarray cannot co-detect balanced structural variants

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EGM in Action

Representative SV and CNV findings from the OhmX™ Platform

Insertion — *KMT2A* Partial Tandem Duplication

KMT2A partial tandem duplications (*KMT2A*-PTD) are cryptic SVs found in ~5–10% of AML cases and are undetectable by karyotyping, FISH, or targeted NGS.

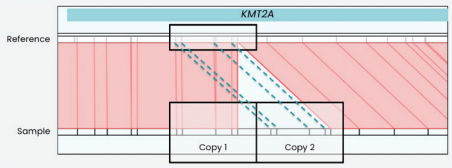

Figure 1. *KMT2A*-PTD in an AML cell line (EOL-1) visualized in Human Chromosome Explorer* (HCE). Copy 1 and Copy 2 in the sample contig (bottom) each align to the same reference interval (top, dashed lines), consistent with a 22 kb tandem duplication at the *KMT2A* locus.

Deletion — *TP53*

TP53 is among the most frequently altered genes in hematological malignancy research. Deletions range from large, karyotype-visible events to small focal alterations below the resolution of many FISH-based approaches.

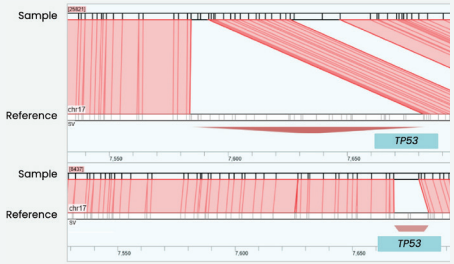

Figure 2. *TP53* deletions in cancer cell line samples visualized in HCE. (Top) 87 kb *TP53* deletion in HL-60. (Bottom) 3.8 kb deletion overlapping exons 7 and 8 in H1299. Deletions are represented as red trapezoids.

Inversion — inv(3)(q21q26)

The inv(3)(q21q26) paracentric inversion involving *MECOM* and the *GATA2* enhancer is a recurrent structural alteration in hematological malignancy research, typically identified by karyotype and confirmed with break-apart FISH.

Figure 3. inv(3)(q21q26) in the MOLM-1 cell line visualized in HCE. (Top) V-shaped arc indicating the intrachromosomal inversion. (Bottom left) Zoomed view at the *GATA2* breakpoint. (Bottom right) Concordant contig alignment at the *MECOM* locus.

Translocation — *RUNX1::RUNX1T1*

The *RUNX1::RUNX1T1* fusion from t(8;21) is a key marker in AML. Both the unaffected homolog and the rearranged allele were resolved in the Kasumi-1 cell line—providing allele-level structural context in a single whole-genome workflow.

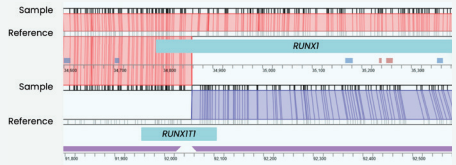

Figure 4. *RUNX1::RUNX1T1* fusion in an AML cell line (Kasumi-1) visualized in HCE. Allele 1 (top) maps to chr21 as the unaffected homolog. Allele 2 (bottom) maps to both chr21 and chr8, indicating the *RUNX1::RUNX1T1* translocation.

Complex Rearrangement — *BCR::ABL1*

Complex rearrangements—defined by three or more breakpoints— are among the most difficult variant classes to resolve with conventional cytogenetics. A single EGM contig (~4 Mb) captured the full architecture of a three-chromosome rearrangement in the K562 CML cell line, spanning chromosomes 9, 13, and 22.

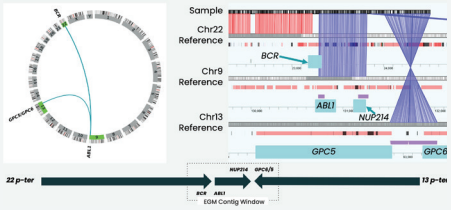

Figure 5. Complex *BCR::ABL1* rearrangement in the K562 CML cell line visualized in HCE. (Left) Circos plot of interchromosomal connections. (Right) Single EGM contig mapping through *BCR* (chr22), *ABL1* (chr9), and *NUP214*/*GPC6/5* (chr13). (Bottom) Breakpoint graph.

Copy Number Variation

EGM data has shown potential for genome-wide copy number profiling. In this example, chromosome-level gains and losses were captured alongside SV detection from the same whole-genome workflow.

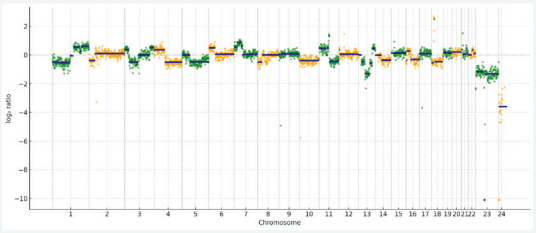

Figure 6. Genome-wide CNV analysis of EGM data from the MEC-1 cell line. Log2 ratios plotted across all chromosomes; black horizontal lines represent segment means; dotted line marks the diploid baseline.[1]

References

1. Stacchini A, et al. MEC1 and MEC2: Two new cell lines derived from B-chronic lymphocytic leukaemia in prolymphocytoid transformation. Leukemia Research. 1999;23:127–136.

* The CNV pipeline is an exploratory research tool under active development. Pipeline outputs have not been analytically validated and are subject to change.

Learn how the OhmX™ Platform can support your hematological malignancy research.

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