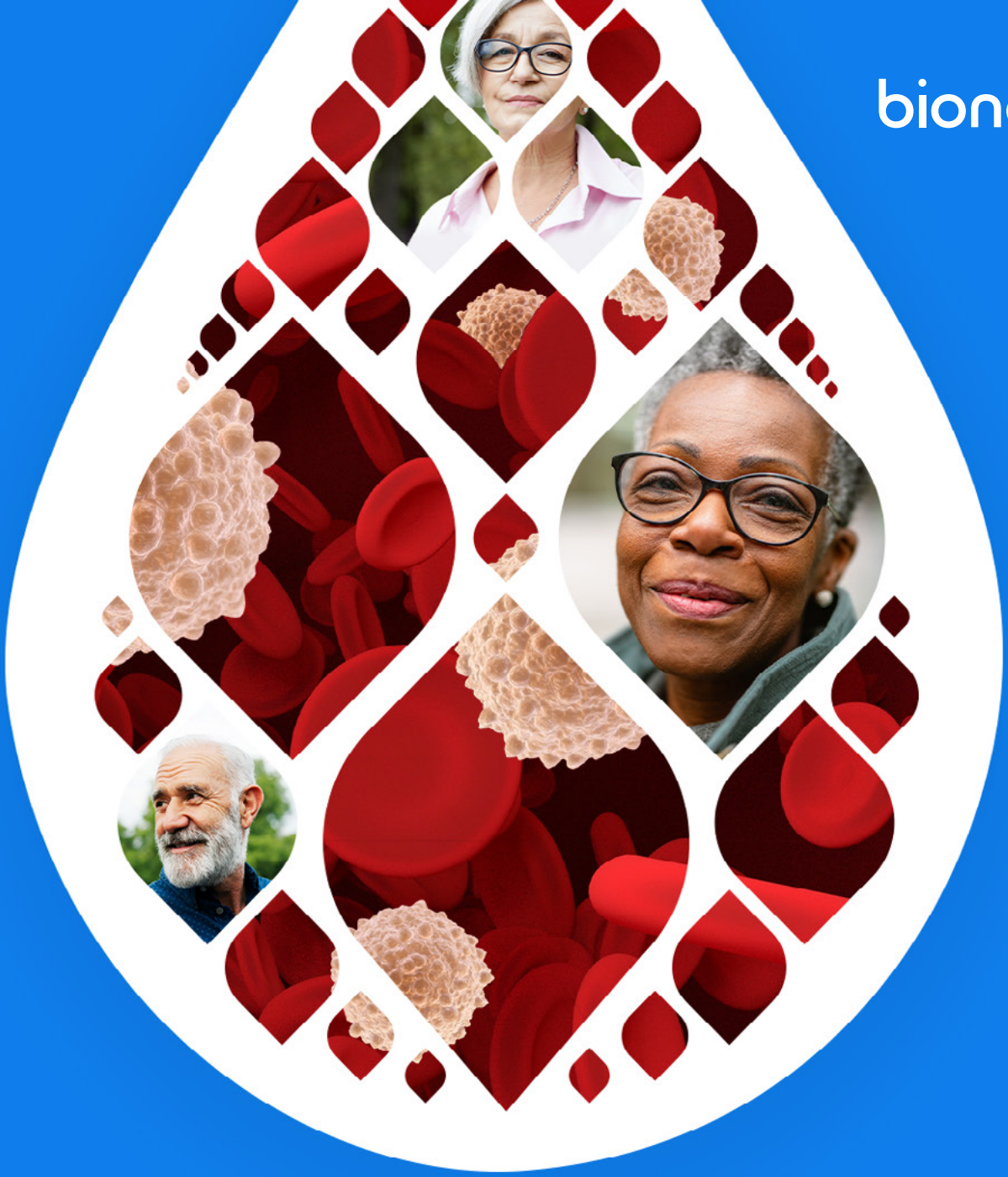
bionano™



REVEAL

key structural variants in hematologic malignancies

A revolution in cytogenomics driven by Optical Genome Mapping.

The State of the Field

Forward from Bionano President and Chief Executive Officer, Erik Holmlin, Ph.D.

Cytogenetics has a problem.

Cytogeneticists are stuck in a cycle where—despite knowing that key pathogenic genomic variants must be present in hematological malignancy samples—they lack proper tools with the power to see many of them. Hematological malignancies are a major driver of cancer mortality and morbidity,[1,2] and cytogenomic analysis is essential to understand the pathology of each case. The task, however, can be daunting, as finding key variants within a hematological malignancy is challenging. This challenge arises largely because the variants are undetectable with many common cytogenomic approaches.[3,4]

Traditionally, researchers in cytogenomics mix and match multiple methods, including karyotyping (KT), fluorescence *in situ* hybridization (FISH), and even microarrays. Together, this widely accepted cytogenomic standard slows cytogenecists down and reduces their discovery power. It's clear that current technologies and workflows underperform when it comes to empowering researchers to move forward.

Problems in the cytogenetic lab lead to problems in the clinic. Advances in genetic analysis can lead to a better understanding of disease etiology. However, without the right tools and workflows for studying structural and numerical variants, I fear that progress will likely be limited. Cytogeneticists deserve to have solutions that meet modern technological capabilities. The field is ready to move forward—to finally reveal critical variants that can drive progress in healthcare.

At Bionano, our goal is to transform the way the world sees the genome in order to assist researchers as they lead the charge in the cytogenomic revolution and breathe fresh life into this critical field. Over the following pages, I hope it will become clear that the field is ready for a new paradigm and that optical genome mapping (OGM) provides the advancement that the cytogenomics field has long awaited. Together, with the skill and knowledge of cytogeneticists and our novel solutions, researchers can finally answer critical questions in biology and medicine and one day be a part of elevating the health of humans worldwise.

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What are Hematological Malignancies?

Hematological malignancies are a complex and diverse set of cancers with origins in blood-forming cells. These devastating diseases have high mortality and morbidity rates,[1,2] but understanding the genomic etiology of the disease can significantly improve outcomes. The key is to identify the underlying genomic abnormalities unique to each patient.

Main Types of Hematological Malignancies

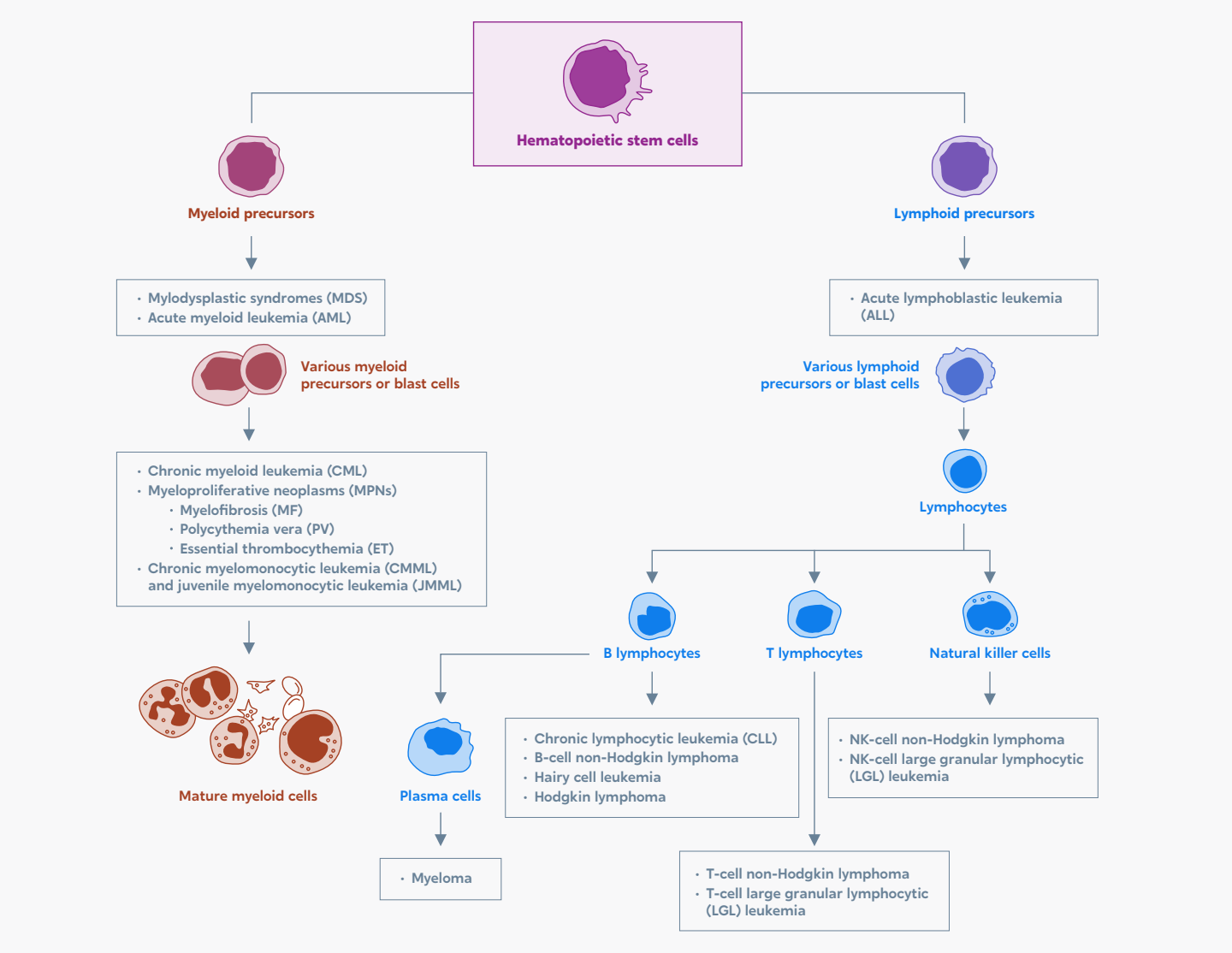


Figure 1. Adapted from the Leukemia Lymphoma Society.[5] Hematological malignancies can arise from a variety of different stem and progenitor cells.

A deeper understanding of the genetic etiology of hematological malignancies could lead to better personalized care and improved outcomes.

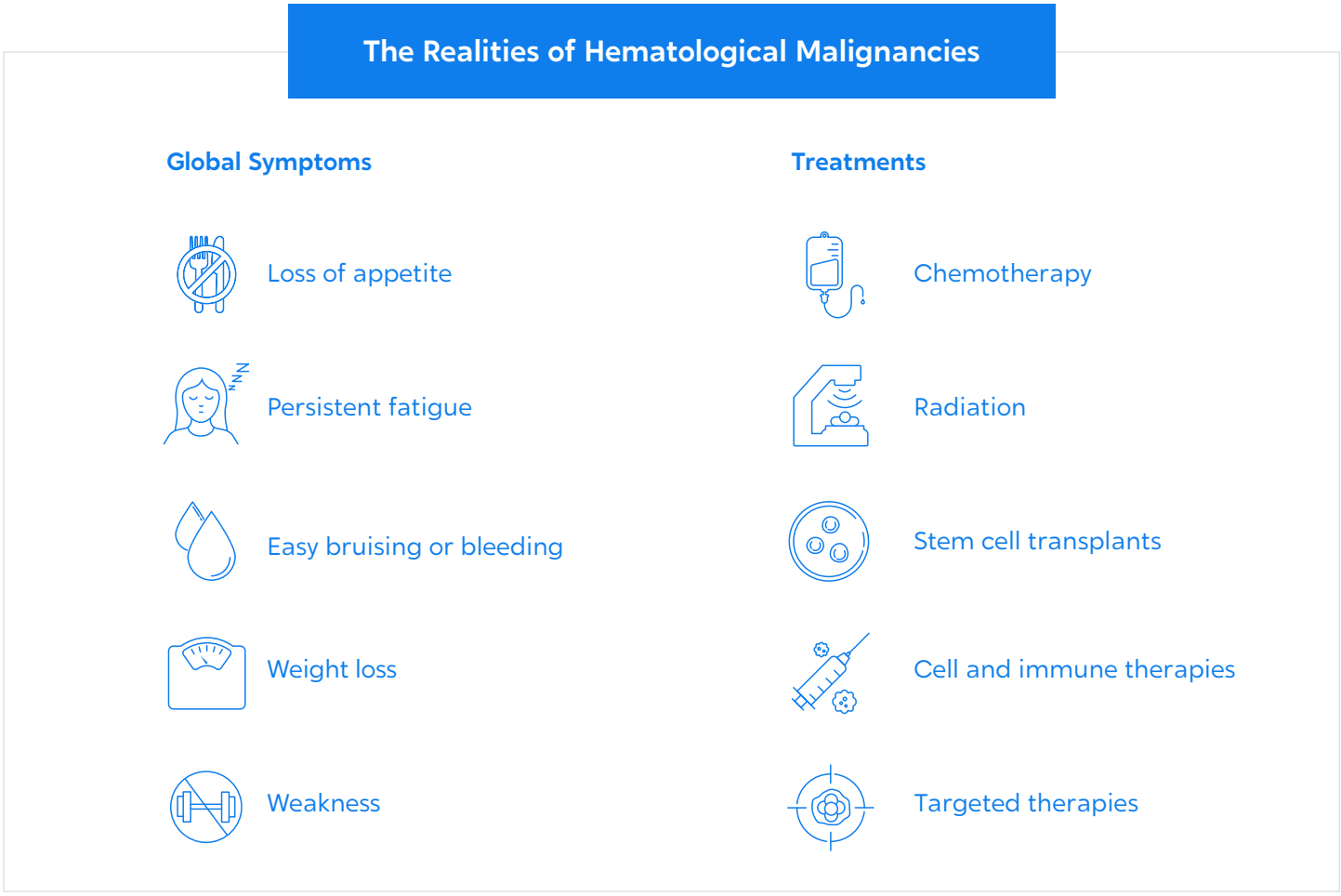


Figure 2. Hematological malignancies are associated with a range of symptoms and treatment options.

A Significant Unmet Need Remains

Despite significant research, there remains a significant gap in understanding hematological malignancies. 50% of tested samples fail to yield a meaningful result due to the low resolution of classical testing approaches.[6-9] Clearly, more work is required to understand the genomic etiology of these diseases.

Section 1 Summary:

New tools and solutions are needed to advance clinical research of hematological malignancies, with the hope that a better understanding of the underlying genomic causes of a disease could, in the future, lead to more personalized treatment options and inform the development of new therapeutics.

Cytogenomic Understanding is Key in Hematological Malignancies

Cytogenomics is essential for understanding the pathology and progression of hematological malignancies. However, many cytogenomic profiling approaches have inherent limitations that may miss actionable insights or make workflows cumbersome. Adding to this challenge is the massive quantity of cases that require genetic analysis and the rapid pace at which medical society guidelines change to include novel biomarkers. Here, we describe the current methodologies for cytogenomic profiling, including optical genome mapping (OGM), an innovative workflow that is revolutionizing the hematological malignancy profiling landscape. Throughout this eBook, we detail the advantages of OGM through real-world experiences supported by peer-reviewed publications.

Structural Variants

Structural variants (SVs) are large chromosomal aberrations that affect the order, orientation, quantity, and chromosomal location of functional elements of the genome, including genes, regulatory elements, and reading frames. While there is no definitive consensus on the minimum size of an SV, it is generally accepted that SVs range from approximately 1,000 base pairs (bp) to a full chromosome. In contrast to single nucleotide variants (SNVs), which refer to single base variants, SVs are larger and can encompass a wide range of structural changes, including copy number alterations.[10] SVs can disrupt gene function and contribute to the onset of cancers and many other diseases.[11,12]

SVs are highly prevalent across hematological malignancies, including conditions like multiple myeloma (MM), chronic lymphocytic leukemia (CLL), and non-Hodgkin lymphoma (NHL).[13] Hematological malignancies have an exceptionally high prevalence in pediatric populations. [13,14]

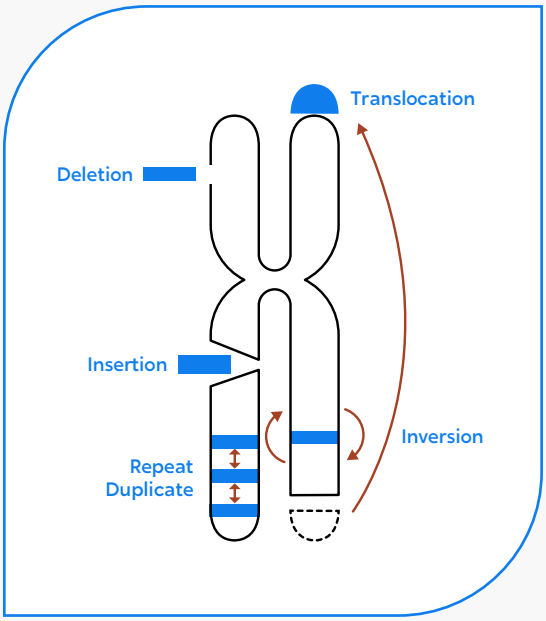
"Structural variants are a very important type of variation in the human genome. And potentially they have been underestimated both in prevalence and in amount that they may explain disease cases."

Alexander Hoischen, Ph.D.
Associate Professor, Genomic Technologies & Immuno-Genomics
Radboud University Medical Center, Departments of Human Genetics and Internal Medicine

The Power of Hematological Malignancy Profiles

Structural and copy number variants are hallmarks of hematological malignancies, and biomedical research is an essential step toward understanding the pathology and progression of these conditions. Research that provides a deeper understanding of the profile of hematological malignancies may:

- Result in an increase in the number of disease samples with meaningful findings
- Provide faster time to genomic insights
- Increase the accuracy of sample risk stratification analysis
- Lead to advancements in healthcare



Cytogenetic Testing is Essential in Hematological Malignancies

- A major cause of hematological malignancies is the presence of chromosomal aberrations.[15]
- The detection of chromosomal aberrations yields insights into tumor pathogenesis.[15]
- In childhood and adolescent AML, chromosomal aberrations are often the only genome variants detected.[16]
- There are over 250 known recurrent chromosomal aberrations in hematological malignancies.[17]

Figure 3. Structural and copy number variants play a prominent role in hematological malignancies, and their detection is essential for furthering hematological research.[15-17]

Guidelines for the Study of Hematological Malignancies

To perform cutting-edge hematological research, understanding up-to-date clinical guidelines, such as those issued by the National Comprehensive Cancer Network (NCCN) and the World Health Organization (WHO), is imperative. Societal guidelines often recommend testing for multiple structural variants in each hematological malignancy and subtype.[18-20] These guidelines provide an important roadmap to assess the cancer case's risk of progression and likely response to therapy, including targeted therapy. However, these guidelines change rapidly, making it difficult for methodologies to maintain pace with current standards. In particular, adapting biomarkers is challenging and expensive for traditional, probe-based approaches, such as FISH.[18-20] Therefore, leading techniques in biomedical research must maintain flexibility to quickly adapt to changing clinical guidelines.

Challenges in Profiling Pathogenic Structural Variants in Hematological Malignancies

Identifying chromosomal abnormalities within a hematological malignancy remains a complex undertaking.[3,4]

As outlined in the key research publications throughout this eBook, it can be challenging to reveal the large variety of structural and copy number variants present in hematological samples—from simple SVs, such as deletions, duplications, translocations, inversions, and aneusomies, to complex chromothripsis. In addition to their varying degrees of complexity, variants can span a wide spectrum of sizes (from hundreds to millions of base pairs) and allele fractions.

It is imperative to have a comprehensive profile of all SV classes within a given sample to identify actionable insights and discover new impactful biomarkers rapidly. Thus, it is desirable for detection methods to handle a wide assortment of chromosomal presentations to provide accurate and valuable insights.

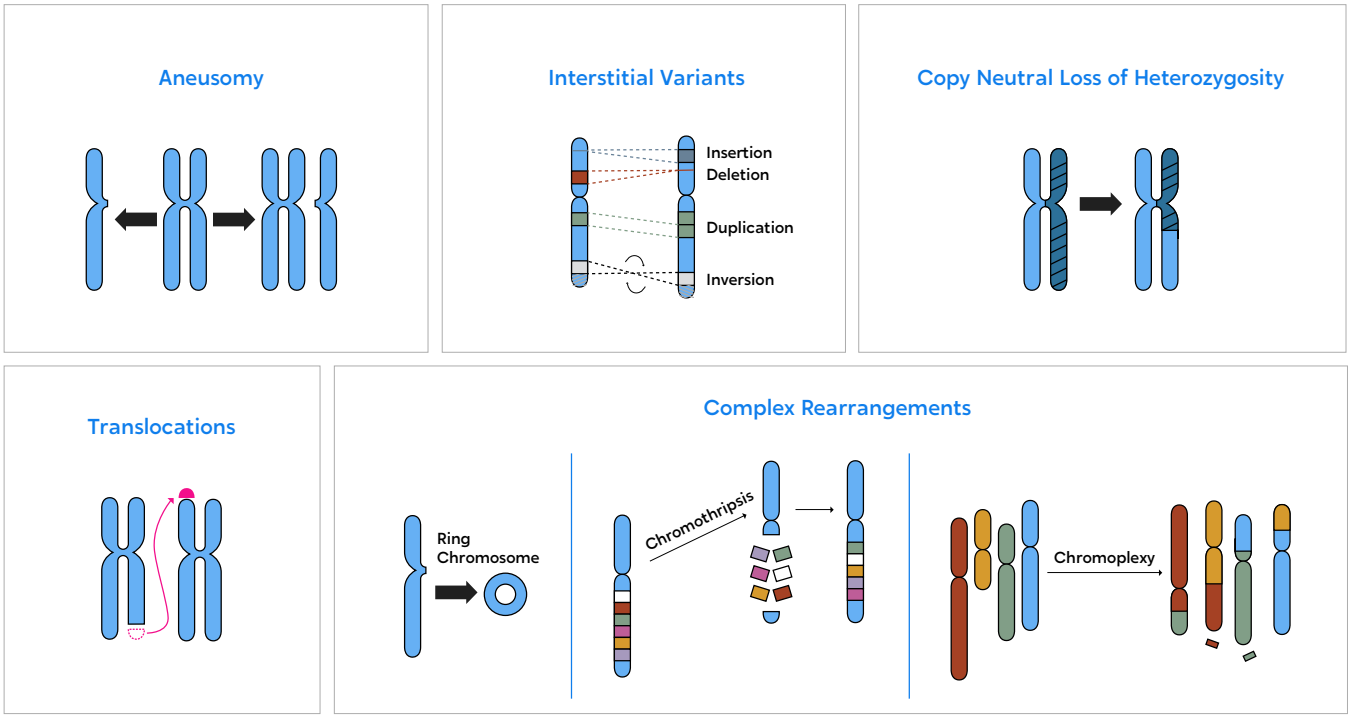


Figure 4. There are a wide variety of structural variants, all of which need to be detected.

Section 2 Summary:

- Structural variants are prevalent across hematological malignancies.
- Correctly identifying these variants is essential to modern hematological research.
- Identifying variants is challenging with current approaches due to their inherent variety and complexity.

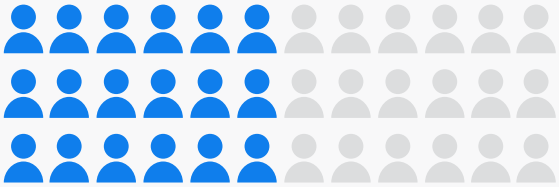
Standard Methods Leave Significant Gaps

As discussed, identifying structural and copy number variants in hematological malignancies is essential. However, many of the standard methods in the cytogeneticist toolbox, such as karyotyping, FISH, and microarrays, have inherent limitations that can impede the identification of critical variants.

"The results of the study demonstrate that we are grossly under-evaluating the degree of genomic aberrations."[21]

Rashmi Kanagal-Shamanna, MD
Associate Professor, Department of Hematopathology
The University of Texas MD Anderson Cancer Center

50% Negative



Multiple studies report that 50% of hematological malignancy samples fail to yield meaningful results.[6-9]

Classical Methods for Identifying Structural Variants

Methodology	Description	Key Limitations
Karyotyping[22–24]	Microscopic examination of the size, shape, and number of chromosomes that produces a genome-wide snapshot of gross genetic changes.	**Resolution:** low resolution (5-20Mbp); many aberrations cannot be resolved visually
		Bias: vulnerable to culture and technician selection bias
		Complexity & Subjectivity: cumbersome workflow requires cell culture and expertly trained cytogeneticists
Fluorescence *In Situ* Hybridization (FISH)[25]	Fluorescent probes hybridize with specific DNA sequences, allowing for visualization of targeted DNA regions.	**Not Scalable:** only one aberration is investigated at a time
		Bias: requires a predetermined set of probes at predefined breakpoints and will miss any untargeted chromosomal alternations
Microarrays[26]	Comparative genomic hybridization and SNV microarrays that detect copy number gains and losses.	**Limited Scope:** only CNVs detected, without structural context; unable to detect balanced rearrangements
		Accuracy: challenges resolving repeat-rich and duplicated regions along with single-copy gains
		Inconsistent: variable performance based on array platform and parameter optimization

Table 1. Overview and key limitations for various standard SV detection methods.[6-9]

Alternative Structural Variant Approaches

Next-Generation Sequencing (NGS)

NGS is a great approach for identifying small specific modifications, such as point mutations, but these techniques often fail to capture larger chromosomal abnormalities.

NGS Methods for Profiling Structural Variants:

- Whole genome sequencing[27]
- Targeted genomics panels[28]

Common Limitations of NGS Approaches[29]:

- Expensive and technically challenging
- Requires manual computational analysis and interpretation
- May miss large-scale structural variations such as inversions, copy number alterations, and translocations
- Targeted panels are biased and only assess a limited, predetermined region of the genome

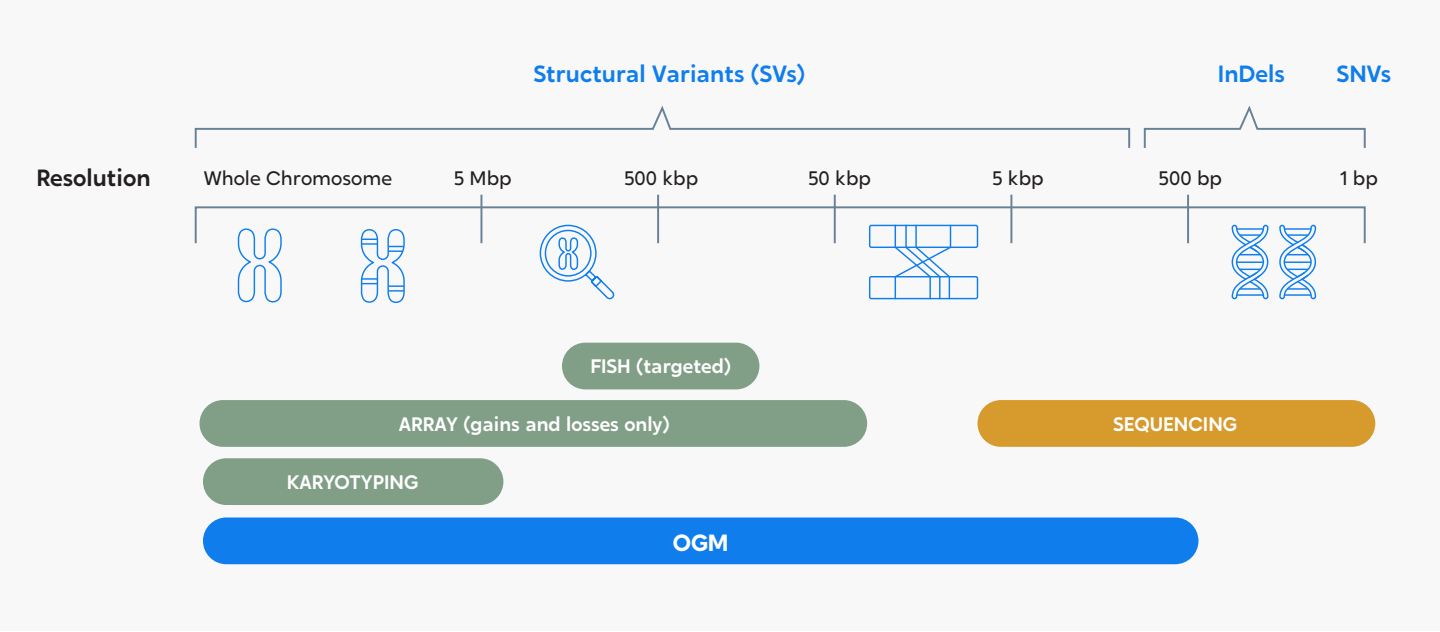


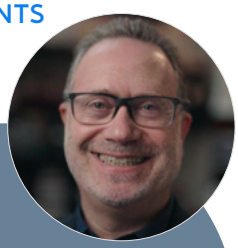
Figure 5. Current classical methods leave a critical gap in the detection of large-scale and often pathogenic SVs.

What Hematopathology Researchers Need in a Detection Method

- A genome-wide approach able to detect all classes of structural variants
- High sensitivity for variants present at low fractions in complex samples
- A robust and efficient protocol with short turn-around-time
- A simple and consolidated process for reporting variants

Technological Limitations Have Negative Consequences

Current approaches limit the research community's ability to accurately and efficiently characterize SVs, leading to poor overall detection rates.[29] Combining multiple approaches is a workaround cytogeneticists use to compensate for the limitations of individual methods. However, this approach (Figure 6) results in complex and cumbersome workflows, which still often miss key variants, as detailed in the case studies highlighted in future sections across this eBook.



"The primary reason that a lot of the structural variation has not been able to be detected in the past really comes from the limited resolution of the standard of care technologies."

Brynn Levy, MSc (Med), Ph.D., FACMG
Professor, Department of Pathology and Cell Biology
Columbia University Medical Center

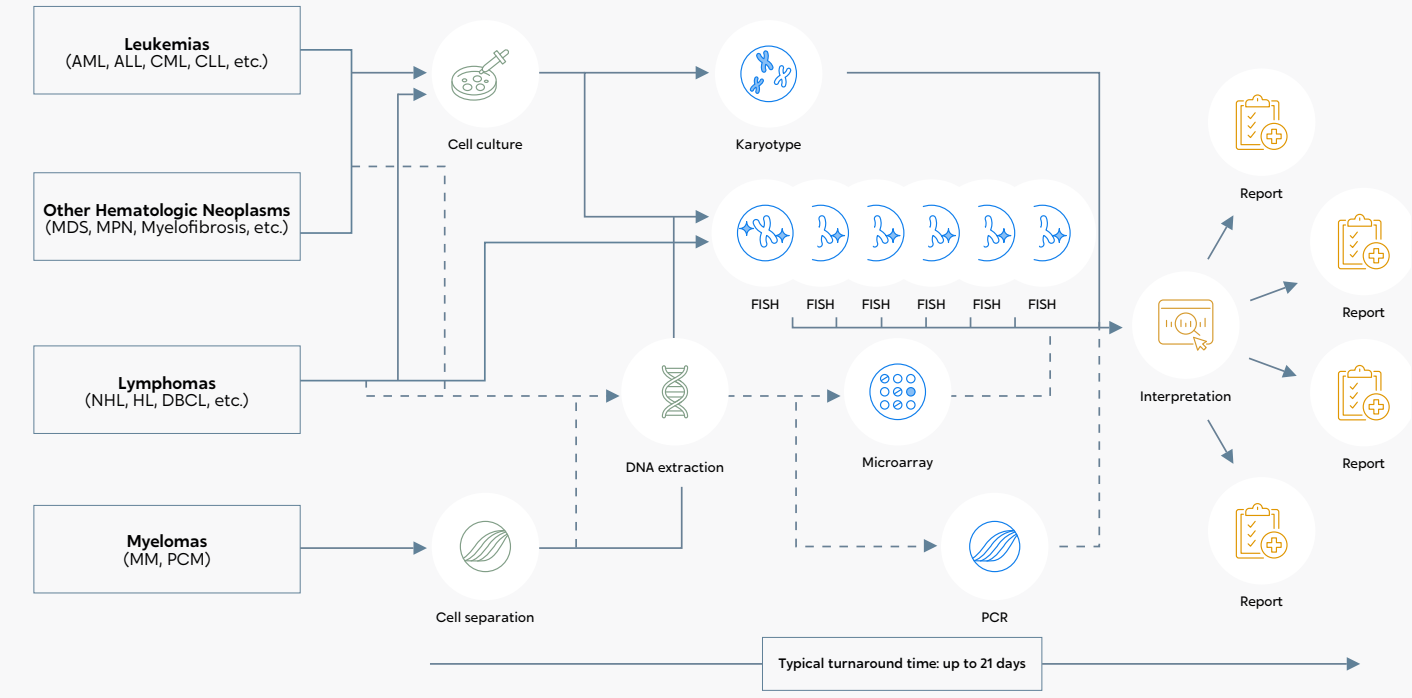


Figure 6. The limitations of current methodologies result in inefficient and inaccurate workflows that require time, money, and specialized expertise.[29]

Section 3 Summary:

- Current approaches require complex integration of multiple techniques, resulting in costly, slow workflows. Even then, many variants are missed or unresolved due to limited resolution and bias.
- Ultimately, these shortcomings present missed opportunities to further hematological research and find actionable insights.[29]
- A new approach to structural variant detection is required in hematology to find more actionable insights and modernize workflows.

What is OGM?

Optical Genome Mapping (OGM) is a powerful new workflow for studying structural and copy number variants that the hematological malignancy research community needs to modernize. OGM combines high-resolution imaging with advanced analytical analysis to provide genome-wide coverage of structural and copy number variants.[30] This paradigm-shifting technique uses ultra-high molecular weight DNA, single molecule imaging, nanotechnology, plus advanced computational analysis to detect all classes of structural and copy number variants in a single, unbiased, and highly efficient assay.[31–33]

"I feel OGM is a perfect technology to bridge the gap between the traditional cytogenetic technologies to identify structure variants and the molecular technologies to identify aberrations at [the] single base pair level."

Rashmi Kanagal-Shamanna, MD
Associate Professor, Department of Hematopathology
The University of Texas MD Anderson Cancer Center

How Does OGM Work?

OGM is a workflow that combines several steps to facilitate visualization and analysis. At a high level, OGM begins by purifying ultra-high molecular DNA to maintain native long-range structure. Then DNA is labeled with fluorophores that bind a motif repeatedly found throughout the genome and linearized in nanochannel arrays. Advanced analytical software uses the fluorescent signals to resolve high-resolution genomic structures from the resulting digitized optical data.

Because OGM spans the full genome, this method is an unbiased and efficient approach to profile actionable structural variants.

Optical Genome Mapping: Transforming the Way Cytogenetics See the Genome

- Spans the full genome
- Combines high resolution with digital analysis
- Unbiased workflow that can detect all classes of SV along with numerical variants, including:
  - Aneuploidy
  - Deletion
  - Duplication
  - Amplification
  - Inversion
  - Translocation
  - Loss of heterozygosity
  - Complex rearrangements

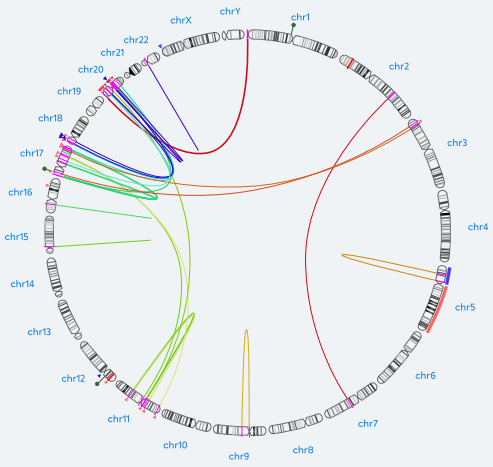
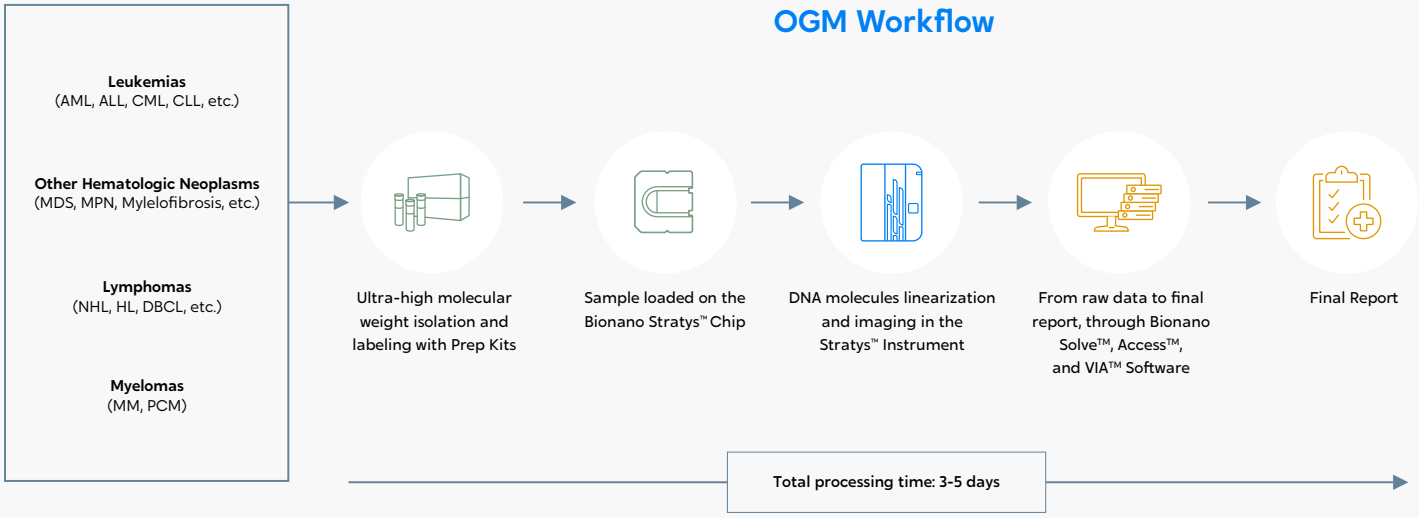


Figure 7. OGM is a next-generation workflow that improves the detection of structural and copy number variants.

OPTICAL GENOME MAPPING AS A TRANSFORMATIVE SOLUTION

Unlike other methods that require extensive cell culture, **OGM is compatible with a variety of primary cell and tissue types**, including:

- Blood
- Bone marrow aspirate
- Cultured cells
- Tissue
- Tumor



Learn more about how OGM works »

Figure 8. The OGM workflow efficiently and accurately resolves all SV types across samples.

	OGM	Karyotyping	FISH	CMA	NGS
Resolution for Structural Variant Detection	Min. SV size: 5kb (>500bp for germline variants)	>5 to 10 Mbp	>100 to 200 kbp	>50 to 100 kbp	1 to ~500bp (short-read) 1bp to ~10kb (long-read)
Detection Bias	Unbiased	Unbiased	Single, targeted probe	Design bias	Sequence bias
Average Turn-Around-Time	<1 week	1-2 weeks	3-5 days	<1 week	Variable
Subjectivity of Analysis	Unbiased	Technician bias	Technician bias	Unbiased	Analysis pipeline bias

Table 2. OGM is an improvement over alternative methods.

OGM Performance Capabilities

OGM provides high-resolution for structural variant detection across hematological malignancies.

Resolution by variant type at >90% sensitivity	
Insertions/Deletions	≥3 kbp
Duplications	≥50 kbp
Translocations	≥70 kbp
Inversions	≥50 kbp

Cancer Analysis Application	
Data Collected	1.5 Tbp
Raw Coverage Tier	400x
Effective Coverage	≥300x
Variant Allele Fraction	≥5%

Table 3. High-resolution and sensitivity of OGM across hematological malignancies. Based on Bionano's Guided Assembly data analysis pipeline for OGM data.[34]

The Advantages of OGM

OGM is already transforming the hematological malignancy landscape by streamlining workflows, uncovering novel, actionable variants, and resolving previously unclear pathologies where other technologies were unable to do so.

"I think the core benefit of OGM is that it combines three technologies in one. So it offers the opportunity to replace Karyotype, FISH and microarrays all in one assay. So as such, our workflow in the laboratory may become much more standardized and easy."

Alexander Hoischen, Ph.D.
Associate Professor, Genomic, Technologies and Immuno-Genomics
Radboud University Medical Center, Departments of Human Genetics and Internal Medicine

Operational Benefits of OGM

OGM radically simplifies the cytogenomic process. Instead of integrating multiple complex, subjective, and technically challenging tests, researchers can use a single OGM assay and achieve greater efficiency. Consolidating methods provides many operational benefits for users, such as:

- Reduced hands-on time
- Faster time to actionable results
- Cost savings associated with running fewer assays
- Simplified operations and training

OGM has other operational benefits, including compatibility with multiple sample types, an inherently unbiased workflow, and reduced overall complexity. OGM is an approachable method that can provide a robust, easy-to-use solution for every lab member.

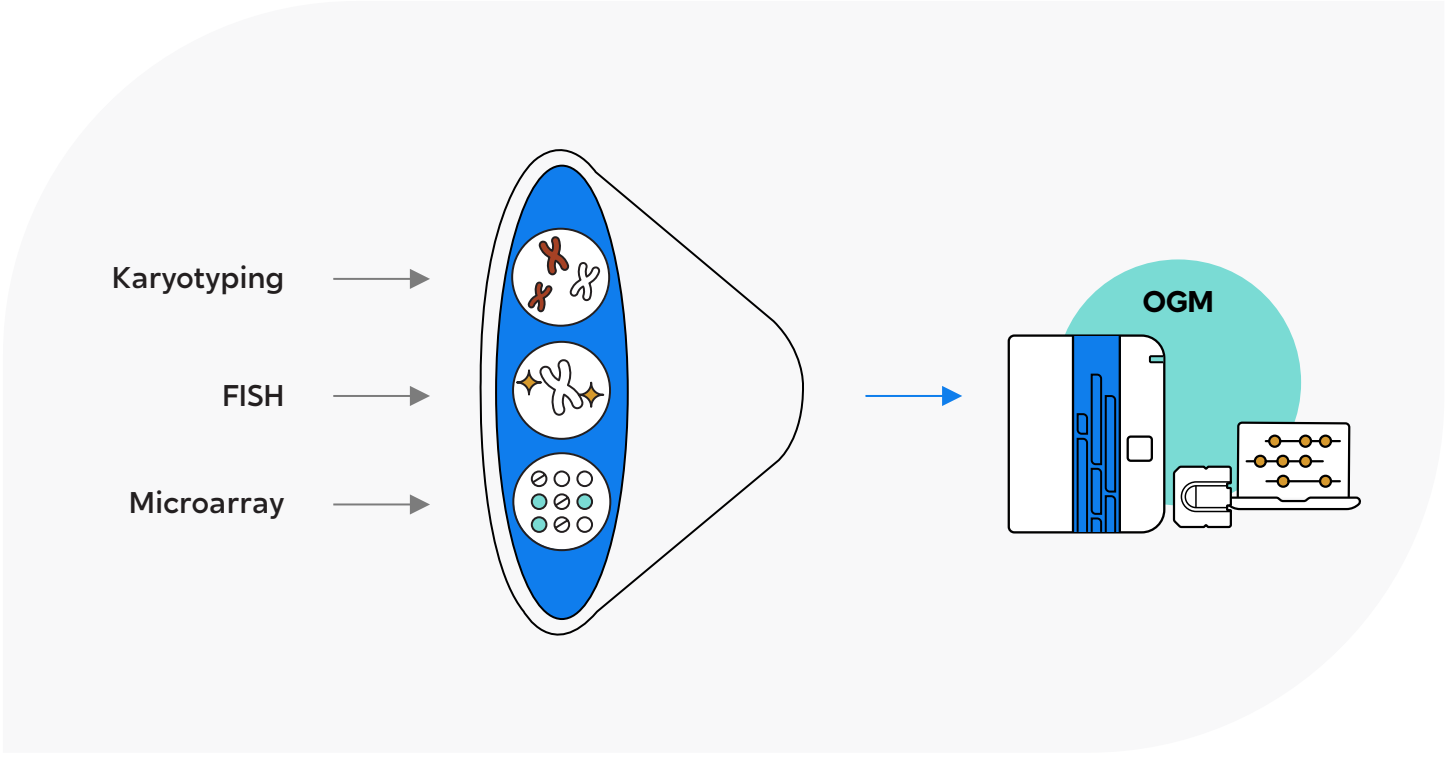


Figure 9. OGM consolidates multiple complex workflows into one approachable assay.

OPTICAL GENOME MAPPING AS A TRANSFORMATIVE SOLUTION

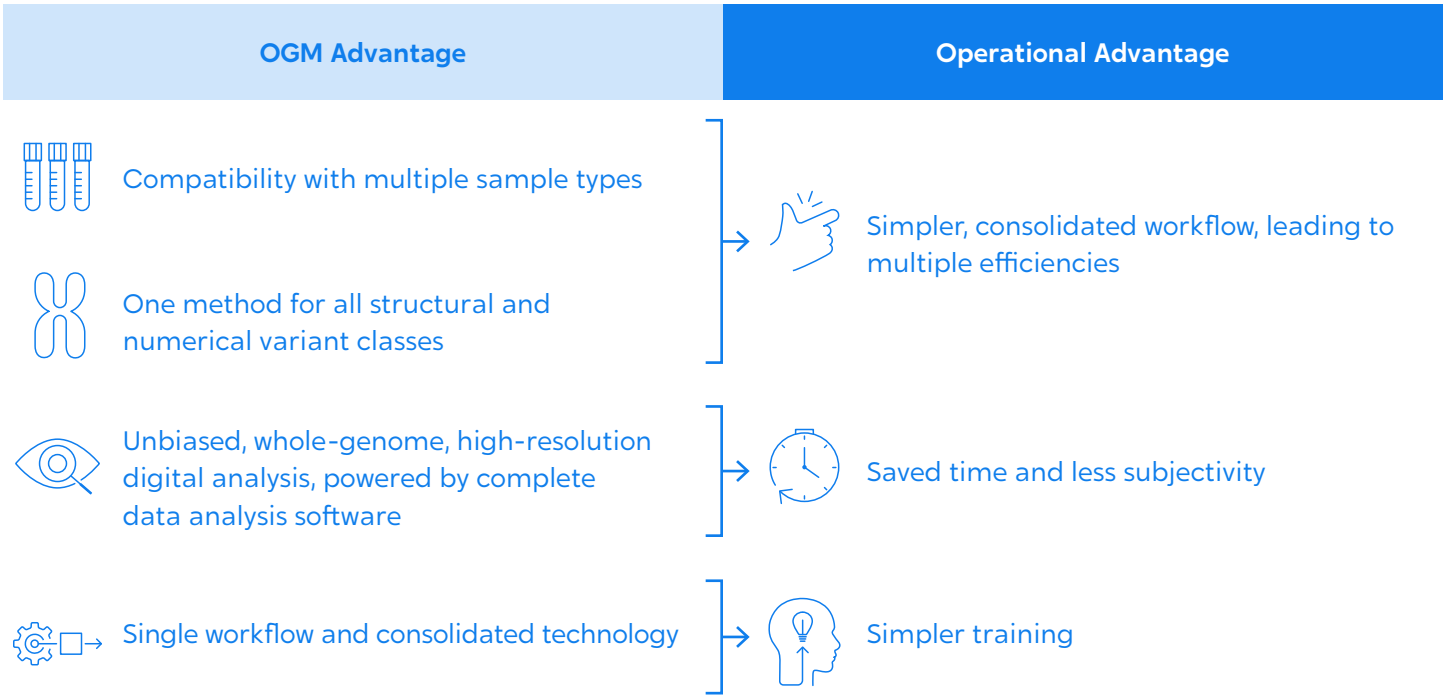


Figure 10. The advantages of OGM workflows have direct implications for laboratory operations.

Clinical Research Benefits of OGM

OGM goes beyond simply consolidating workflows to aid operational logistics. In fact, OGM shows great potential for enhancing clinical research by aiding in the detection of structural and copy number variants beyond those identified with alternative methods.[21,35]

There is a preponderance of evidence supporting the ability of OGM to match alternative methods.[36] In addition to OGM's high concordance with leading detection practices, evidence also suggests OGM is capable of detecting structural and copy number variants that these methods routinely fail to detect.[21,35-39]

Unlike alternative methods, which are often limited in their ability (Table 1), OGM can reliably resolve all classes of structural and copy number variants, including complex SVs.

"30% of previously unsolved cases for B-ALL, which previously underwent karyotype + FISH + microarray + NGS, were solved using OGM."

Gordana Raca, MD, Ph.D., FACMG[40]
Director of Clinical Cytogenomics,
Center for Personalized Medicine Department of Pathology and Lab Medicine
Children's Hospital Los Angeles
Professor, Clinical Pathology
Keck School of Medicine at the University of Southern California

OPTICAL GENOME MAPPING AS A TRANSFORMATIVE SOLUTION

This ability to identify pathogenic and actionable structural and copy number variants can be traced back to the same features that provide extensive operational benefits — its unbiased, whole-genome, modern approach. The power of OGM has the potential for paradigm-shifting clinical implications for the future of hematological malignancies. Clinical research using OGM may lead to solutions that help solve unresolved cases across hematological malignancies, improve risk stratification, and ultimately result in better patient outcomes.

OGM Advantage	Clinical Research Advantage
Robust, reliable, and accurate structural and copy number variant detection	High concordance with classical methods
Unbiased screening across the entire genome	Detection of novel variants
Higher resolution and sensitivity	More actionable insights
Greater sample stratification capabilities	More accurate stratification and prognostic risk assessment

Figure 11. The advantages of OGM workflows have direct implications for clinical research.

"With OGM we are changing subjectivity to objectivity in going from a visual microscope-based karyotype to a high-resolution digital output."

Adam C. Smith, Ph.D., FCCMG, FACMG, erCLG

OGM Shows High Concordance with Other Methods

Studies have shown that OGM has high concordance with traditional methods such as karyotyping and FISH.[21,35-39] Additionally, OGM has the resolution to identify large-scale structural and copy number variants that NGS approaches struggle to recognize.[21,35] Taken together, these characteristics position OGM as a premier solution to identifying all SV classes with accuracy and efficiency.

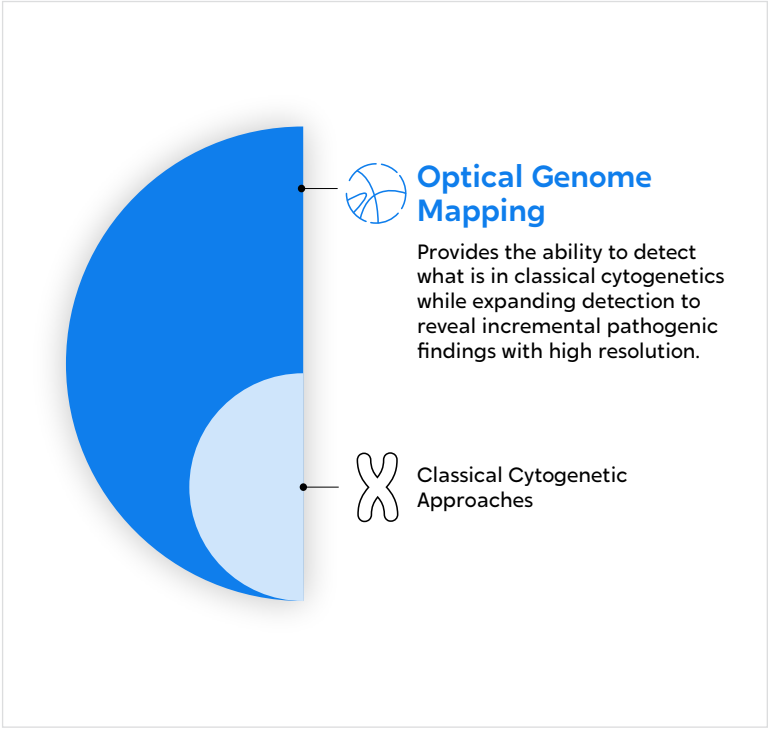


Figure 12. OGM encompasses many of the benefits of classical cytogenetic methods with the additional ability to detect variants missed by other methods.

KEY PUBLICATION 1

BLOOD ADVANCES

OGM not only matches classical technologies but has the power to uncover additional relevant variants in 13% of cases.

Optical Genome Mapping in Acute Myeloid Leukemia: A Multicenter Evaluation[37] »

OGM was 100% concordant with standard methods when evaluating a cohort of 100 acute myeloid leukemia (AML) cases. In 13% of cases, OGM identified additional and often actionable pathogenic findings.

OPTICAL GENOME MAPPING AS A TRANSFORMATIVE SOLUTION

KEY PUBLICATION 2

JOURNAL OF MOLECULAR DIAGNOSTICS

OGM represents a viable alternative to classical methods, providing high concordance and improved pathogenic insights.

Clinical Validation and Diagnostic Utility of Optical Genome Mapping for Enhanced Cytogenomic Analysis of Hematological Neoplasms.[41] >>

An analysis of 69 well-characterized, unique samples with OGM resulted in high concordance with 99.2% accuracy, 100% specificity, and 98.7% sensitivity, compared to classical methods. OGM analysis also identified several SVs that other approaches missed.

OGM Resulted In:

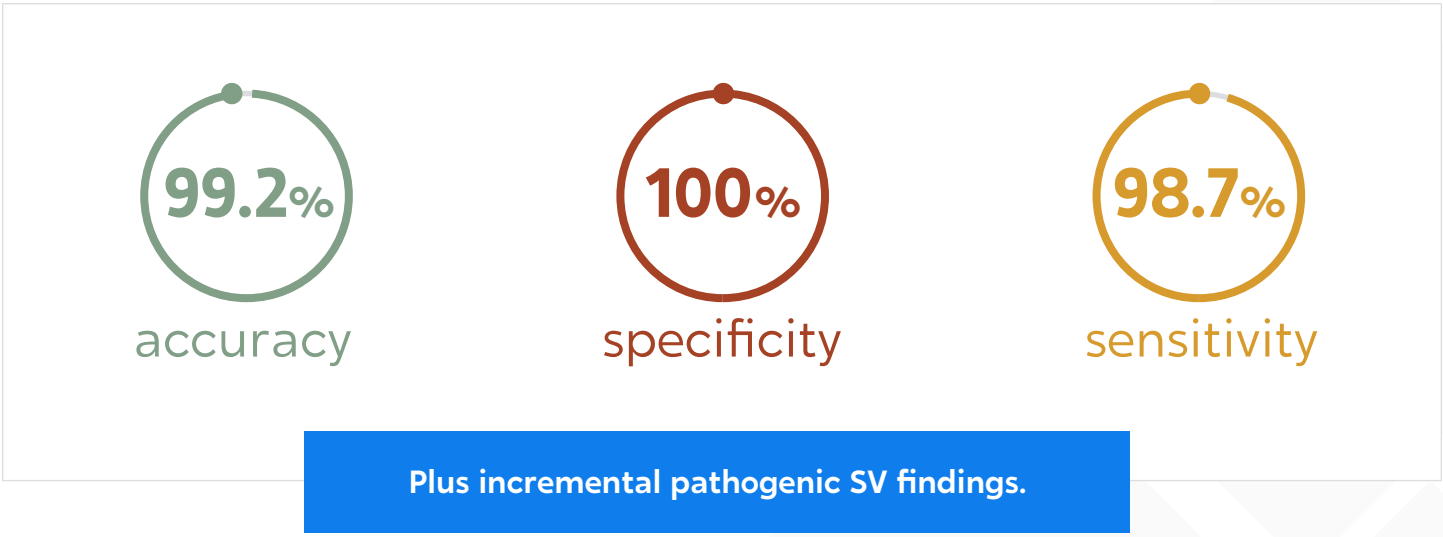


Figure 13. Adapted from Sahajpal et al., 2022.[41] OGM provided high concordance with traditional methods.

	Cohort Size	Clinical Referral	Number of Abnormalities Included (Classical Methods)	Concordance with Cytogenetic Results
1 University of Oulo[42]	18	CLL	16	**100%**
2 Multi-site AML Consortium[37]	100	AML	190	**98.4%**
3 Augusta, Emory[41]	69	CLL, AML, MDS, MM, lymphoma, PCM, CML, ET and others	164	**99%**
4 M.D. Anderson[21]	101	MDS	194	**99%**
5 CHU Amiens[43]	10	B and T ALL	78	**97%**
6 Johns Hopkins University[44]	5	Leukemia/Lymphoma and Solid Tumors	30	**100%**
7 University Hospital Olomouc[45]	11	Multiple myeloma	172	**98%**
8 Radbound University[36]	48	AML, MDS, CML, CLL, ALL, MM, MPN, T-PLL, LYBM	112	**100%**

Table 4. Numerous studies validate OGM's excellent concordance with other approaches.

OGM Enhances SV Detection

Many studies suggest that OGM finds structural and copy number variants that were missed by other approaches and frequently identifies novel SVs.[21,35]

OGM led to incremental pathogenic findings in:

34% of samples
Yang et al., 2022

13% of samples
Levy et al., 2023

33-54% of samples
Balducci et al., 2022

Figure 14. When OGM is used, novel pathogenic SV findings are often detected.

KEY PUBLICATION 3

LEUKEMIA

OGM can improve the identification of pathogenic variants.

High-Resolution Structural Variant Profiling of Myelodysplastic Syndromes by Optical Genome Mapping Uncovers Cryptic Aberrations of Prognostic and Therapeutic Significance.[21] >>

OGM detected 383 significant, recurrent, and novel SVs — nearly twice as many SVs as chromosome banding analysis (CBA). Of the 383 clinically significant aberrations, more than half were cryptic to CBA. (Figure 15, below).

OPTICAL GENOME MAPPING AS A TRANSFORMATIVE SOLUTION

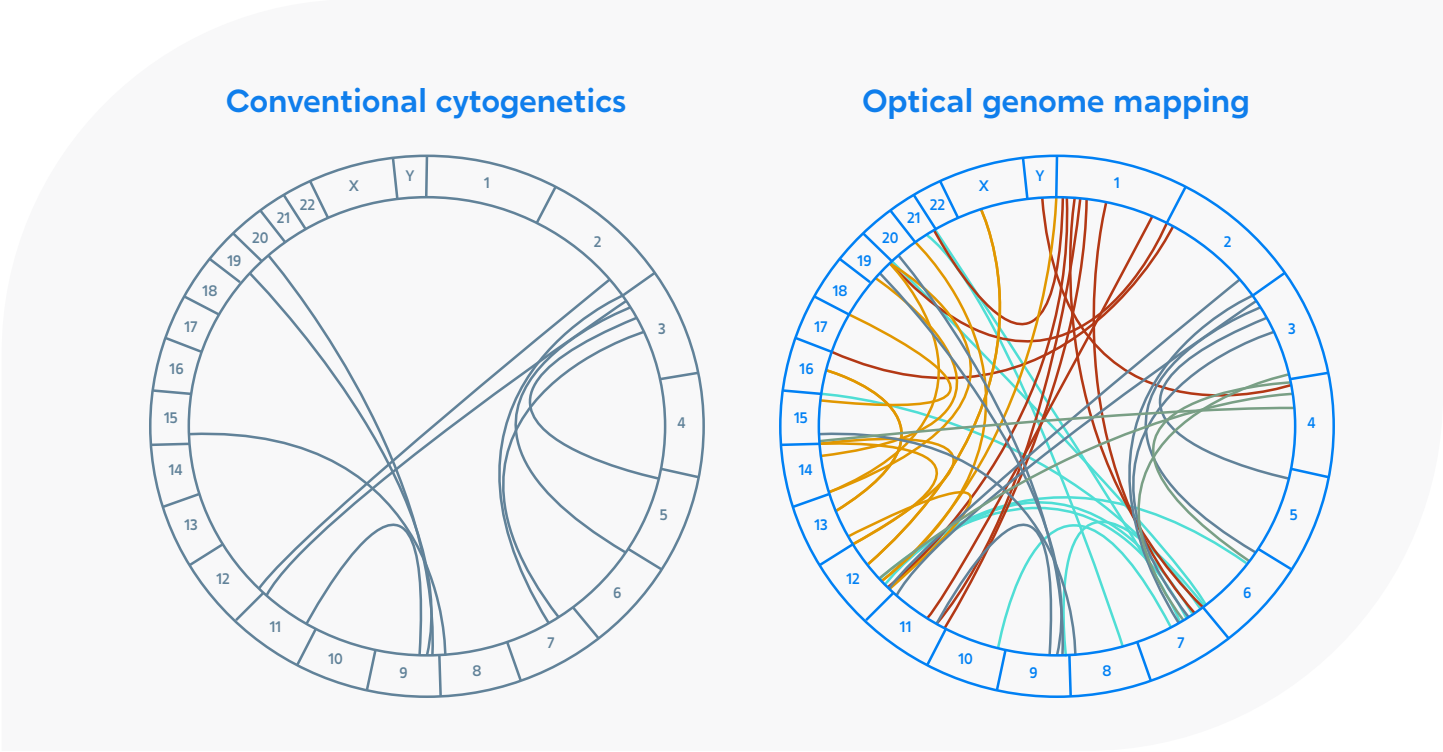


Figure 15. Adapted from Yang et al., 2022.[21] Comparison between the results of conventional cytogenetics, specifically chromosomal banding analysis (CBA) and optical genome mapping (OGM). OGM detected nearly twice as many SVs as CBA.

OGM led to overall 31% more
SVs detected, compared to KT and FISH

Gerding et al., 2022

OGM detected twice as many
SVs as traditional methods

Yang et al., 2022

Figure 16. When OGM is used, novel SV findings are often detected, compared to traditional methods.

KEY PUBLICATION 4

THE AMERICAN JOURNAL OF HUMAN GENETICS

OGM resulted in a more complete assessment than other single assays and has the potential to replace classical cytogenetic approaches and rapidly map novel leukemic drivers.

Next-Generation Cytogenetics: Comprehensive Assessment of 52 Hematological Malignancy Genomes by Optical Genome Mapping.[36] >>

Samples from 52 individuals with hematological malignancies were processed. OGM detected 19 novel gene fusions and revealed higher complexity than previously recognized.

OGM Has the Ability to Better Resolve Complex Karyotypes

Cytogenetic methods such as FISH and karyotyping struggle to resolve many complex SVs, such as novel fusions and chromothripsis and fail to compensate for inherent genome complexity.[46] These limitations leave critical actionable SVs undiscovered. OGM, with its genome-wide approach and digital precision, can confidently and consistently profile challenging SVs.[37]

"OGM reveals more of what matters: more clinically relevant SVs, leading to higher success rates and resolution of unsolved cases."

Laïla El-Khattabi, MD
Hôpitaux de Paris
(AP-HP)-Université de Paris

KEY PUBLICATION 5

SCIENTIFIC REPORTS

OGM has the potential to resolve complex genomic architectures in hematological malignancies.

Whole-Genome Optical Mapping of Bone-Marrow Myeloma Cells Reveals Association of Extramedullary Multiple Myeloma with Chromosome 1 Abnormalities.[45] >>

This study used OGM to refine large intrachromosomal rearrangements on chromosome 1 and associate them with extramedullary progression.

KEY PUBLICATION 6

CANCERS

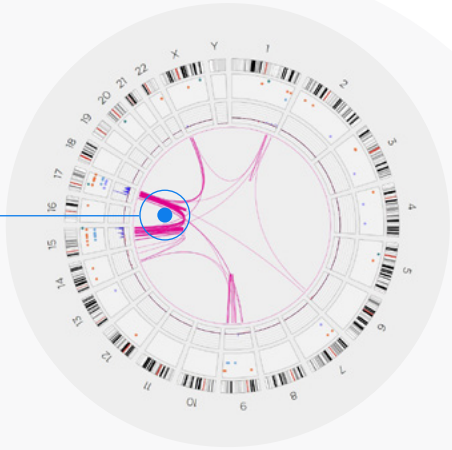
OGM is a powerful approach to characterize complex karyotypes with improved resolution.

TP53 Abnormalities are Underlying the Poor Outcome Associated with Chromothripsis in Chronic Lymphocytic Leukemia Patients with Complex Karyotype.[46] >>

OGM was used to study the genomic complexity of chronic lymphocytic leukemia patients with chromothripsis. OGM characterized these complex karyotypes and improved the resolution of chromothripsis.

Complex Rearrangements

Multiple clustered fusions within and between chromosome 15 and 17, with copy number losses and focal amplifications



Abnormal Ploidy

Copy neutral loss of heterozygosity, in multiple chromosomes with baseline CN

Copy number gain and aneusomy; multiple chromosomes with CN=4

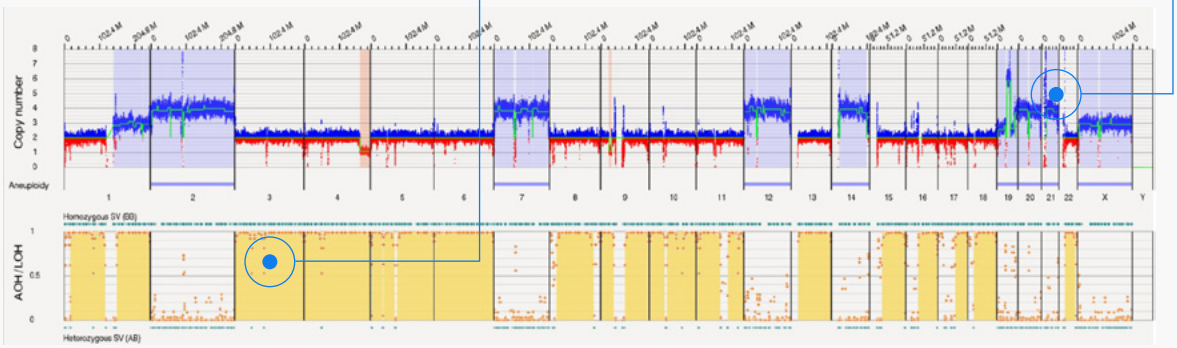


Figure 17. Optical genome mapping can resolve many classes of structural variants, including complex variants such as complex rearrangements and abnormal ploidies.

OGM Has the Potential to Improve Risk Stratification

As demonstrated in many published studies, OGM exceeds the current detection standard for hematological malignancies. Improved detection has the potential to provide profound implications in the future for improving risk stratification.[21,35,37,38]

"The more data we can get, the more informed decisions we can make, and optical genome mapping provides an amount of data that isn't available through other techniques."

Ravindra Kolhe, MD, Ph.D., FCAP
Professor and Interim Chair, Pathology
Associate Dean, Translational Research
Associate Director, Genomics,
Georgia Cancer Center
Leon Henri Charbonnier Endowed Chair of Pathology
Medical College of Georgia

KEY PUBLICATION 7

AMERICAN JOURNAL OF HEMATOLOGY

OGM increased the detection rate and cytogenetic resolution and may provide better sample stratification and inform more accurate understanding.

Optimizing the Diagnostic Workflow for Acute Lymphoblastic Leukemia by Optical Genome Mapping.[47] »

Here, the authors analyzed 41 acute lymphoblastic leukemia cases and found that OGM identified all recurrent copy number alternations and structural variants, and for 8% of samples, OGM findings resulted in a change in ELN or R-IPSS score.

OGM is the Next Revolution in Cytogenomics

OGM meets the current standards of cytogenomics while filling the gaps left by traditional methods. Unlike approaches such as karyotyping and FISH, OGM provides an objective, high-resolution view of the genome. OGM also provides the structural resolution required to identify structural and copy number variants often missed by NGS. As cytogenomics continues to move forward, the capabilities and advantages of OGM stand out as a powerful solution for researchers.

OGM Improves Cytogenomic Profiling

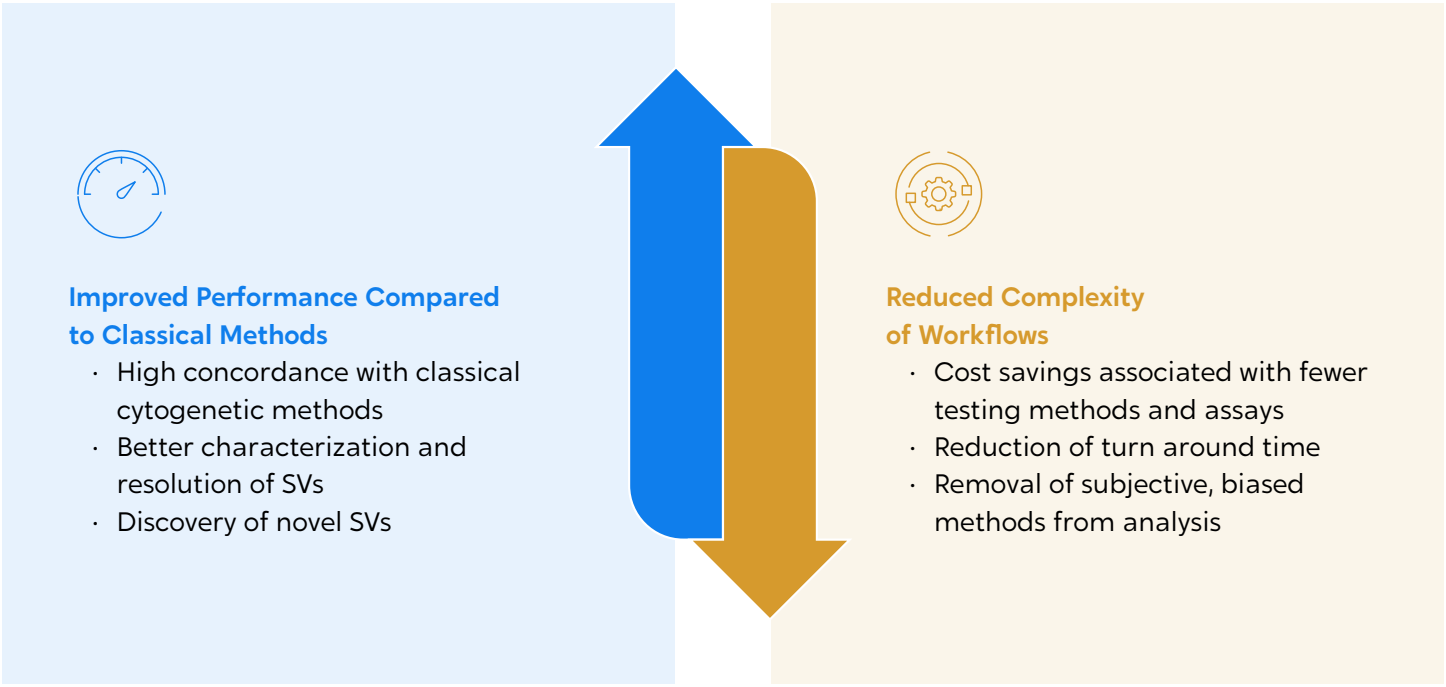


Figure 18. The advantages of OGM for hematological cytogenomic profiling.

Section 4 Summary:

- OGM is a completely new approach for studying structural and copy number variants that combines high-resolution imaging with advanced analysis.
- OGM provides operational and clinical research advantages, such as efficient and cost-effective workflows, genome-wide coverage, and detection of all classes of structural and copy-number variants.
- OGM is highly concordant with classical methods while enhancing variant detection.

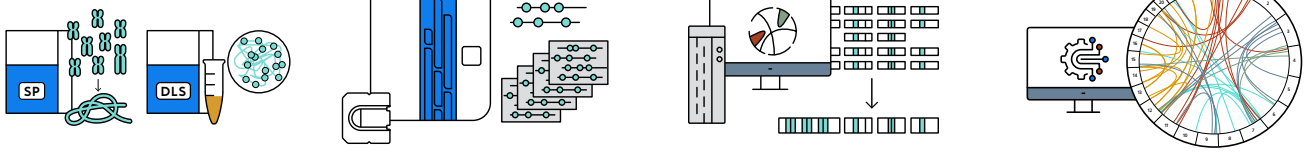
Reach a New Level of Workflow Speed and Simplicity

Reveal all classes of structural variants and leave the limits of traditional cytogenetics and sequencing behind with Optical Genome Mapping and the Bionano Stratys™ System.

Bionano Sample Preparation Kits | Stratys™ Chips | Stratys™ System | Stratys™ Compute | Bionano VIA™ Software

The OGM Workflow

1 PREP → **2 IMAGE** → **3 COMPUTE** → **4 INTERPRET**



BIONANO PREP KITS

Isolate ultra-high molecular weight (UHMW) DNA. Label and stain specific sequences across the entire genome.

STRATYS™

Load labeled DNA into chip for scanning. Linearize and image labeled and stained DNA in repeated cycles to scan copies of the whole genome.

STRATYS™ Compute

Algorithms align molecules to reference genome to construct consensus maps and call all classes of structural variants genome-wide.

VIA™

Tertiary analysis software to visualize, interpret, and report OGM data.

Experience the Benefits of the Stratys

- **High Sample Capacity**
- **Ultimate Flexibility**
- **"Jump the Queue" for Priority Samples**
- **Reduced Turnaround Time**
- **Accelerated Computation with NVIDIA RTX GPUs**

Click here to learn more about the Stratys™ System. >>

Transforming the Future of Cytogenomics with OGM

The future of cytogenomics is bright with Bionano. Researchers can consolidate their process from cumbersome, multi-method integrations into a seamless, end-to-end OGM workflow. The straightforward OGM approach empowers teams to optimize their time, creating efficiencies where other methods create challenges.

Not only does OGM simplify workflows for teams, but it also increases genomic insights. OGM has repeatedly demonstrated its ability to exceed standard methods. It is no wonder OGM bridges the gaps left by other approaches — OGM is an objective, unbiased, whole-genome method with digital precision. With OGM in their toolkit, researchers will find new structural and copy-number variants with a lower cost and operational burden.

"The things we can do using this technology, the discoveries, the identification of biomarkers, prognostication, improving therapy, identifying targets, [they're] endless. The potential is endless, and I'm super excited to work with this in the future."

Rashmi Kanagal-Shamanna, MD
Associate Professor, Department of Hematopathology
The University of Texas MD Anderson Cancer Center

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