bionano GENOMICS

CYTOGENOMICS

REVOLUTIONIZING CYTOGENOMICS

CONSOLIDATE TRADITIONAL CYTOGENETIC ASSAYS INTO A SINGLE WORKFLOW

10,000x
greater resolution
compared to karyotyping

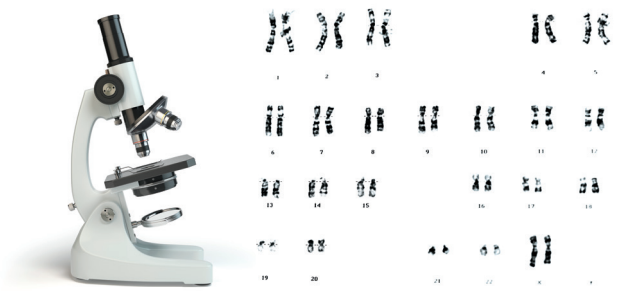
In spite of the revolution sequencing technologies have brought about for genomics research and diagnostics, it has barely modified the way cytogenomic labs look at structural variants. While NGS identifies single nucleotide variants along with small insertions and deletions (<150 bp), it fails to identify most large insertions, deletions, and copy-number variations in repetitive regions of the genome. In addition, NGS does not reliably detect balanced SVs such as inversions and translocations. Moreover, NGS relies on short-read sequences that are mapped to a reference human genome introducing a bias while calling structural variants. Long-read sequencing is still limited in its resolution.

These limitations make direct visualization of the DNA the most reliable approach for the identification of structural variants to date. Unsurprisingly, the way structural variants are detected in clinical samples has minimally evolved over in the past decades and mainly rely on traditional cytogenetic methods such as karyotyping, Fluorescent in situ Hybridization (FISH) and array based technologies. None of these methods alone can address complex cases due to technical limitations and need to be combined and complemented with molecular methods such as MLPA, qPCR, RNAseq to provide a complete therapeutic and prognostic assessment of the patient or tumor genome.

Bionano Genome Imaging visualizes the genome similarly to how karyotyping is performed: the direct visualization of patterns of marker banding on intact DNA molecule. Only here, we apply 500,000 such bands to a genome, and the imaging is performed in an extremely high throughput, automated manner in nanochannel arrays that linearize megabase size molecules. This allows us to see events at 10,000x greater resolution than by karyotyping: insertions and deletions at 500 bp, vs ~5 Mbp by chromosome banding analysis. With 1600x of genome coverage collected per sample, we can detect structural variants down to 1% variant allele fraction (VAF).

CYTOGENETICISTS

Visualize patterns on intact DNA molecules to detect structural variation



SAPHYR®

Automates the imaging of 1000x more label patterns on intact DNA molecules to detect Structural Variation in massively parallel nanochannel arrays

bionanogenomics.com/cytogenomics

BIONANO PROVIDES HIGHLY SENSITIVE DETECTION OF ALL STRUCTURAL VARIANT TYPES

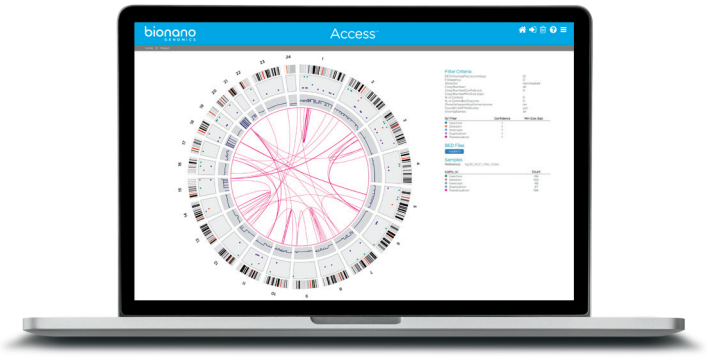
Validation studies around the world are confirming Bionano's performance. To date, Bionano found 100% of all clinically reported variants detected by karyotyping, FISH and microarray combined, and revealed many that were missed.

A large collaborative, multi-center study led by Columbia University is comparing Bionano with the standard of care for heme malignancies: preliminary results presented during a Cancer Genomics Consortium webinar in May 2020 showed 100% concordance with karyotyping on all 91 samples analyzed, and with array and FISH on the subset of samples where those tests were performed.[1]

A study by MD Anderson Cancer Center compares Bionano's performance vs traditional cytogenetic methods in Myelodysplastic Syndrome (MDS) patients. Early results on 13 MDS samples show 100% success in detecting variants at 10% allele fraction and higher compared to karyotype and array, and many additional variants and complexities discovered that were missed by cytogenetics methods.[2]

Another team of scientists led by Dr. Alexander Hoischen from Radboud University Medical Center (RUMC) in the Netherlands reported successful validation of Bionano Genomics' Saphyr® system for the clinical analysis of leukemia genomes. The study, published in bioRxiv, found that Saphyr was 100% concordant with the standard of care for the detection of somatic chromosomal abnormalities. A total of 48 patient samples with a combination of myeloid and lymphoid leukemias, representative of the most common referrals to the RUMC clinic, were analyzed using standard cytogenetic analysis. All samples had an allele fraction of the pathogenic variants of at least 10%. 37 samples were considered simple and 11 samples were categorized as complex, based on the number of large structural abnormalities. When all 48 samples were subsequently analyzed with Bionano, the team was able to identify all previously reported aberrations. In addition, Bionano allowed for a better resolution and a more complete picture of complex aberrations. A complex chromothripsis structure was resolved unambiguously and in other cases, additional fusions were identified, or marker chromosomes of unknown origin were resolved.[3]

Several other studies are ongoing, so far all with similar preliminary results.



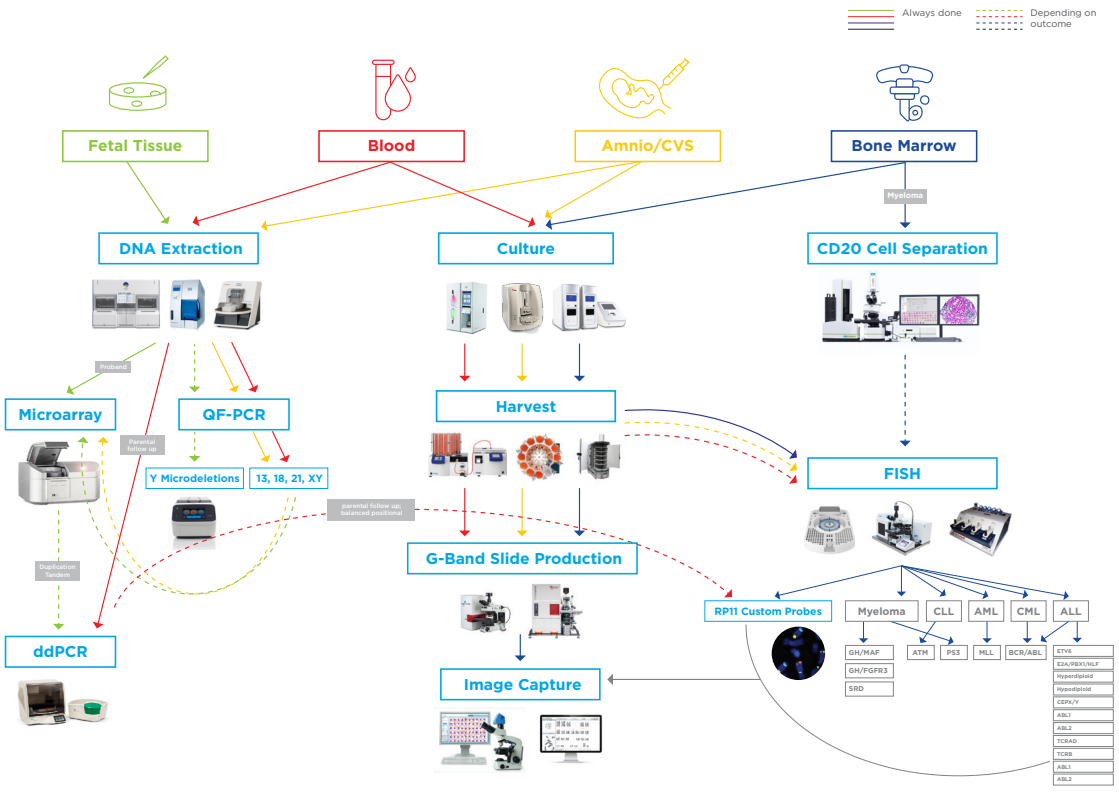
Method	Resolution	Features[4]
Karyotyping	~5-10 Mbp	Extensive training required for interpretation, slow, labor intensive data collection and analysis. Cell culture required.
FISH	~100 kbp	Targeted, extremely limited approach; only shows handful of variants; slow, labor intensive data collection
Array based techniques	~50 kbp	Cannot detect balanced rearrangements; Cannot resolve nature of a structural aberration
Bionano Saphyr	**500 bp**	**Fully automated detection of: CNVs, repeat expansion disorders, FSHD, unbalanced events from single exon level to aneuploidies, balanced events, inversions, translocations, gene fusions down to 1% VAF**

BIONANO CONSOLIDATES THE TRADITIONAL CYTOGENETIC ASSAYS INTO A SINGLE WORKFLOW

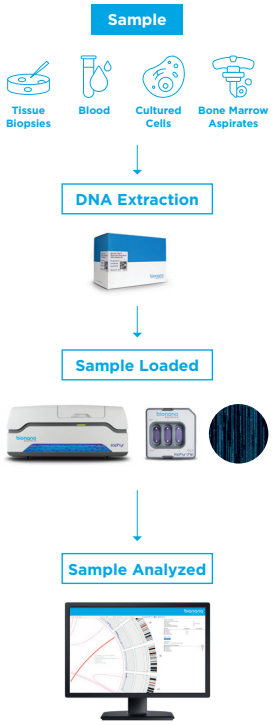
Bionano Saphyr is the ONLY technology that allows for the highly sensitive detection of all structural variant types, even those present at low allele fraction in heterogenous cancer samples, in an unbiased genome-wide manner.

By providing a complete and unambiguous picture of the genome structure, it can identify prognostic markers not currently monitored, and enable a complete characterization of the cancer or patient genome in single test, **replacing multiple cytogenetic tests that make up the gold standard**.

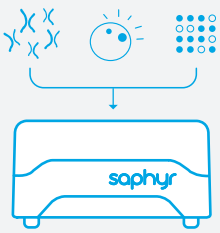
Current Cyto Lab Workflow



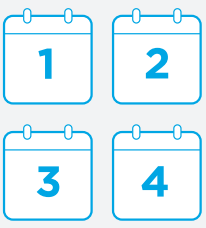
Bionano Workflow



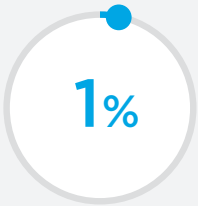
EXPERIENCE THE ADVANTAGES OF SAPHYR



Consolidate 3 assays into 1 workflow



Sample to results in 4 days



Variant allele fraction detection

coverage per sample

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3 WAYS TO GET BIONANO DATA

GET THE SERVICE

BIONANO DATA SERVICES

Submit your samples to Bionano Data Services and receive an appropriately filtered set of structural variant calls. SV data is presented using the Bionano Access® visualization software. Files can be exported in the format of your choice.

The Bionano Support team will work with you on experiment design and analysis training. Full analysis is available as an option.

Sample Types Accepted – Frozen, Mammalian Only

- Tissue Biopsies
- Blood
- Cultured Cells
- Bone Marrow Aspirates

Pricing

- $950 per genome
- $1,150 per genome for mosaic/cancer samples collected at 400x
- Upon request for mosaic/cancer samples collected at 1600x

GET THE CONSUMABLES

REAGENT RENTAL AGREEMENT

Run samples in-house with a Saphyr® Instrument free of charge for the duration of your project. The Bionano Support team will install the Saphyr System and provide training on sample preparation, instrument operation, and data analysis.

Pricing

- $550 per genome with commitment of 120 genomes per 6 months (includes DNA isolation, labeling, chips and Bionano Compute On Demand)
- Installation and training included

GET THE SAPHYR SYSTEM

SYSTEM AND CONSUMABLES PURCHASE

Purchase the Saphyr System for your institution without any reagent commitment. The Bionano Support team will install the Saphyr System and provide training on sample preparation, instrument operation, and data analysis.

Saphyr System Components

- Saphyr Instrument
- Saphyr Chips
- Bionano Prep Kits
- Bionano Access Server
- Bionano Access Software
- Bionano Compute On Demand (optional)

Pricing

- Saphyr System starting at $150,000
- $550 per genome
- $450 per genome with 240 genome bundle
- Installation and training included

To see all cytogenomics case studies, presentations and additional materials, visit bionanogenomics.com/cytogenomics

References: 1. Dr. Brynn Levy, CGC 2019 Series 2. Dr. Rashmi Kanagal-Shamanna, AMP 2019 Series – Dr. Rashmi Kanagal-Shamanna 3. Neveling K et al. bioRxiv 2020.02.06.935742 4. Hastings et al. European guidelines for constitutional cytogenomic analysis, European Journal of Human Genetics, 2019.

Contact your Bionano Regional Business Manager to get started.

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