bionano GENOMICS

GENETIC DISEASE RESEARCH

GENOME-WIDE DETECTION OF ALL STRUCTURAL VARIANTS

down to
1%
Variant allele fraction

Advances in sequencing technologies have barely changed the way structural variants are detected.

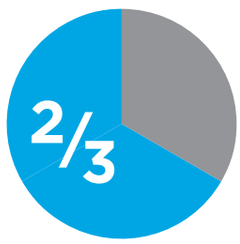
NGS relies on short-read sequences that are mapped to a reference human genome and fails to identify most large insertions, deletions, and copy-number variations in the 2/3rds of the genome that is repetitive. In addition, NGS does not reliably detect balanced SVs such as inversions and translocations.

Bionano Genome Imaging directly visualizes patterns of labels on intact DNA molecules to detect structural variation.

Bionano Genome Imaging detects balanced translocations, repeat expansions, events flanked by repeats, and even rearrangements of large segmental duplications. Every type of structural variant is detected with sensitivities as high as 99%, and with Positive Predictive Value (PPV) of more than 97%.

Unlike sequencing based methods, that are typically unable to detect insertions or identify where the extra sequence is inserted, Bionano detects both deletions and insertions starting at 500 bp with high sensitivity. And because it uses a single molecule imaging technology, mosaic variants down to as little as 1% variant allele fraction can be detected.

Mega-base size molecules are isolated from blood, cells, tissue or tumor biopsies, and a single enzymatic reaction places 500,000 fluorescent labels all throughout the genome at a specific sequence motif. The labeled DNA molecules are linearized in nanochannel arrays on the Saphyr chip and imaged in an extremely high throughput, automated manner. Changes in the patterning or spacing of the labels are detected automatically, genome wide, to call all structural variants.



2/3 of the human genome is repetitive

99%
SV detection sensitivity

97%
PPV

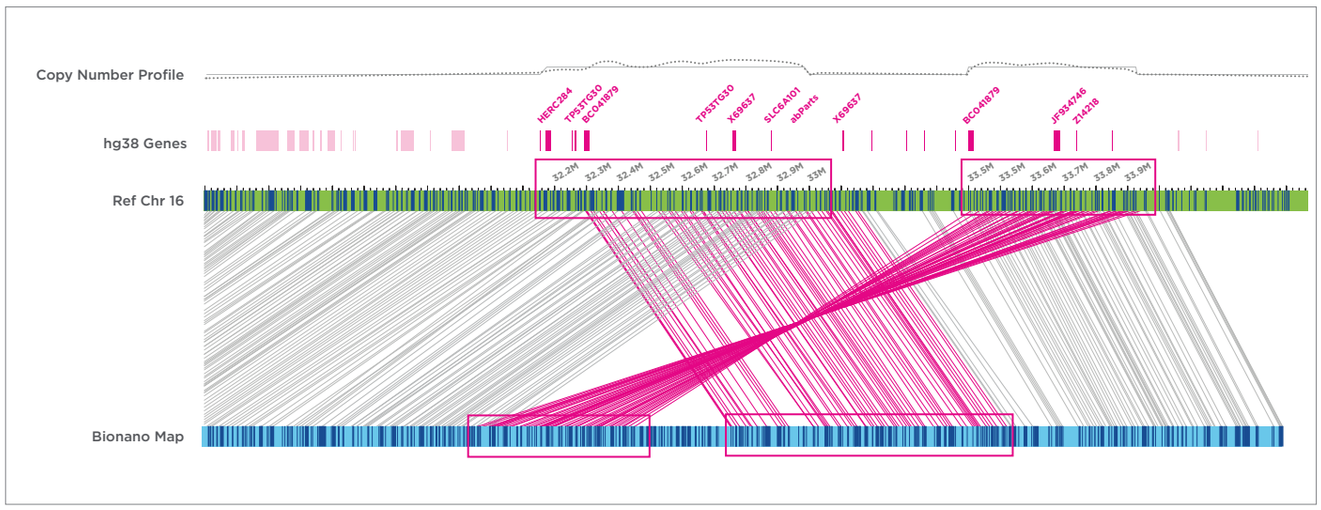
500 bp
Starting size for detection of deletions and insertions

1%
Variant allele fraction detection

bionanogenomics.com/geneticdiseases

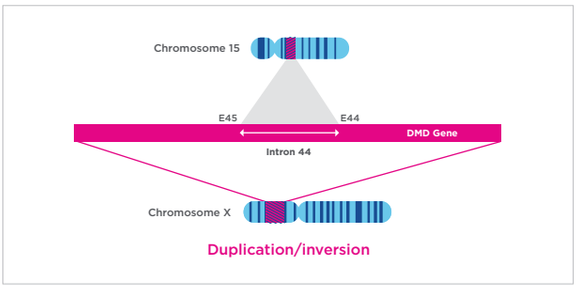
BIONANO FINDS NEW CANDIDATE GENES

In a newborn with Congenital Diaphragmatic Hernia (CDH), a severe developmental disorder affecting the diaphragm, lungs and sometimes heart, Bionano detected two adjacent duplications, one direct and one inverted. Bionano revealed a much more complex architecture than could be inferred from microarray data and identified several additional candidate genes for CDH.[1]



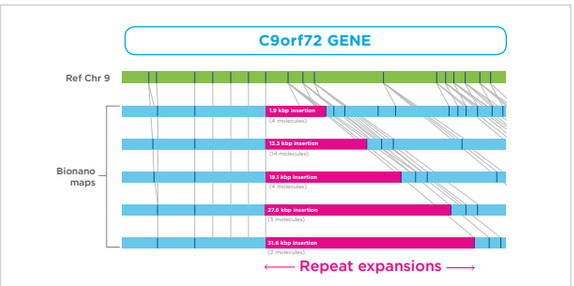
BIONANO FINDS NEW VARIANTS IN KNOWN GENES

In a patient with Duchenne Muscular Dystrophy (DMD), a 420 kbp segment from chromosome 15 was duplicated in an inverted orientation in intron 44 of the Dystrophin gene. This insertion was not detected by NGS, and while chromosomal microarray can detect the duplication, its location and therefore implication in DMD could not be determined.[2]



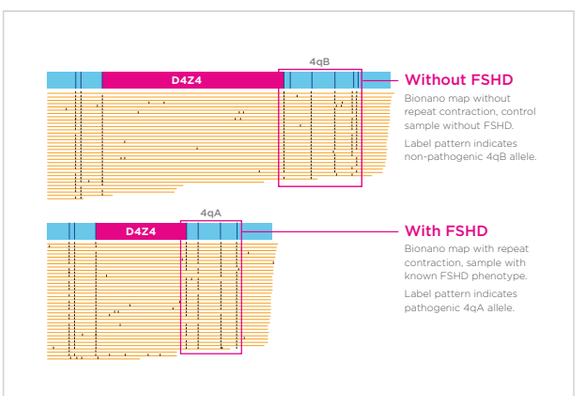
BIONANO REVEALS REPEAT EXPANSIONS

In a single postmortem brain sample from ALS patient, Bionano Bionano detected a highly mosaic range of expansions of the C9orf72 GGGGCC repeat, ranging from the reference allele to a 32 kbp expansion. No modern technology has been capable of spanning and measuring these large C9orf72 repeat expansions.[3]



BIONANO CAN DETECT FSHD

Facioscapulohumeral Muscular Dystrophy (FSHD) is a common form of muscular dystrophy with an extremely complex genotype. Correct genotyping requires the accurate sizing of a very large repeat region in the subtelomeric region of chromosome 4, a correct determining of the pathogenic vs non-pathogenic allele, and the distinction between the chromosome 4 repeat and an almost identical repeat on chromosome 10 not related to the disease. Molecular methods fail to do so, and hence a cumbersome, imprecise Southern Blot is currently used to molecularly diagnose this disease. The Bionano EnFocus FSHD Analysis performs the entire detection automatically, and validation studies have shown perfect concordance with the gold standard method.[4]

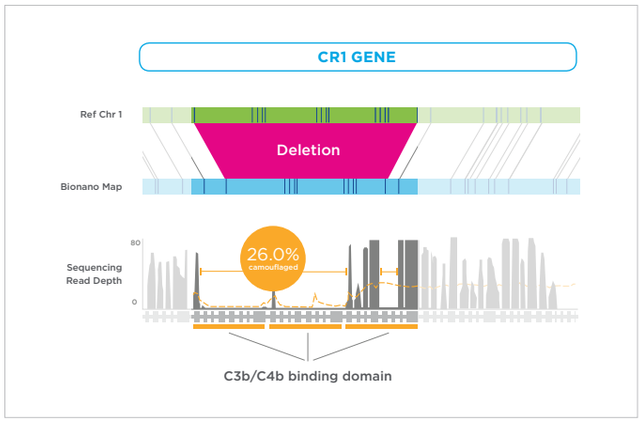


For Research Use Only. Not for use in diagnostic procedures.

BIONANO FINDS VARIANTS OTHER TECHNOLOGIES CAN'T SEE

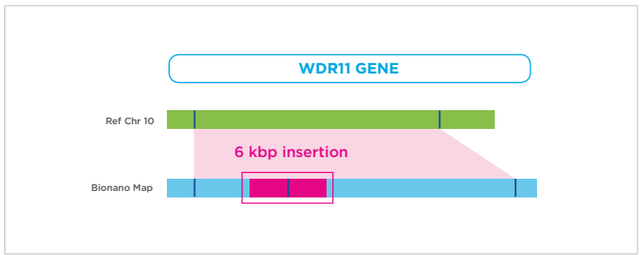
Because they're camouflaged:

Many protein-coding exons are 'camouflaged' in NGS datasets because of variably-repeated binding domains—the exons occur in more than one gene or in tandem within the same gene, making correct alignment of short reads impossible. Bionano allowed for the direct measurement of the number of C3b/C4b binding domains for each haplotype in CR1, an Alzheimer-associated gene, in this patient with Alzheimer's Disease.[3]



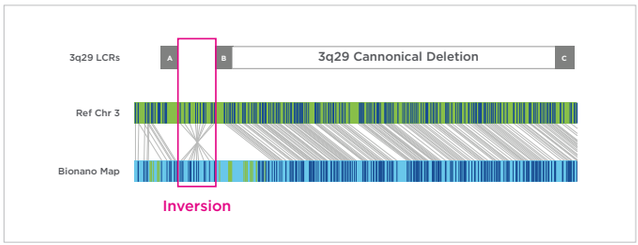
Because they're insertions:

While deletions are somewhat easier to detect by NGS, insertions are rarely picked up from NGS data. In a genetic male patient with gonadal dysgenesis, Bionano identified a 6 kbp insertion in the WDR11 gene, associated with abnormal testes development and cryptorchidism.[2]



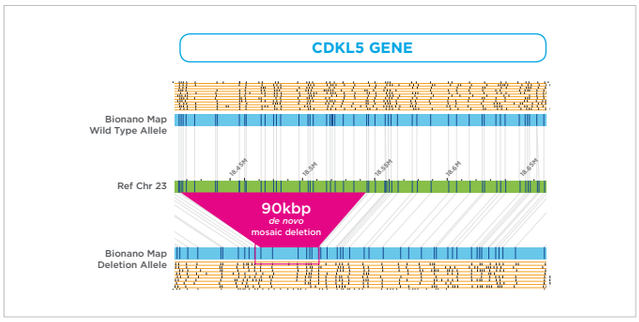
Because they're flanked by segmental duplications or are in other complex regions of the genome:

3q29 Microdeletion syndrome is present when a 1.5 Mbp region between two segmental duplications (also called Low Copy Repeats (LCR)) is deleted. It is thought that inversions in the parents between LCRs in this region predispose to the deletion in the child. Here, Bionano detected a 350 kbp inversion between LCR A and B, something that's not been possible with any other genome analysis technology.[5]

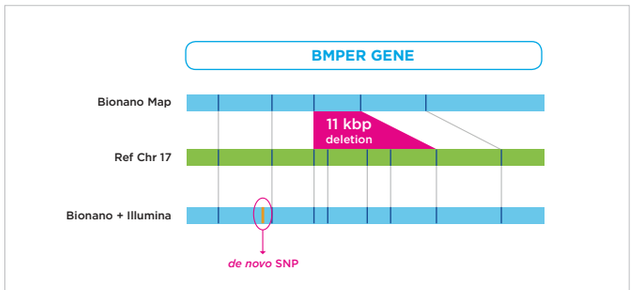


Because they're mosaic:

A juvenile patient with epilepsy, hypotonia and developmental delay, extensively studied as part of the Undiagnosed Disease Network, remained undiagnosed. Bionano found a 90 kbp mosaic deletion in CDKL5, an X-linked gene essential for normal brain development and function, and a phenotype that perfectly matches the patient's. The wild type allele is shown on top, the deletion allele below.[2]



BIONANO CAN BE COMBINED WITH NGS



To find compound heterozygous mutations:

In a patient with a complex phenotype and a variety of growth and developmental defects, Bionano detected a 11 kbp deletion in the *BMPER* gene inherited from the mother, while a *de novo* SNP in the same gene was detected on the other allele. This combination creates a compound heterozygous mutation, only detected by a combination of NGS and Bionano.[2]

BMPER is an autosomal recessive gene that regulates the Bone Morphogenetic Protein (BMP) and the phenotype matched a potential *BMPER* disruption.

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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, Human Only

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

Pricing

- $650 per genome
- $750 per genome for mosaic/cancer samples

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

Prices in local currency are available upon request.

To see all genetic disease case studies, presentations and additional materials, visit bionanogenomics.com/geneticdiseases

References: 1. Dr. Frances High, ASHG 2019 Series – Dr. Frances High 2. Dr. Hayk Barseghyan, Bionano Symposium at ASHG 2019 – Hayk Barseghyan 3. Dr. Mark Ebbert, ASHG 2019 Series – Dr. Mark T. W. Ebbert 4. Dr. Alka Chaubey, ASHG 2019 Series – Dr. Alka Chaubey 5. Dr. Jennifer Mulle, Bionano Symposium at ASHG 2019 – Jennifer G. Mulle

Contact your Bionano Regional Business Manager to get started.

info@bionanogenomics.com | +1.858.888.7600 | bionanogenomics.com

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