BioNano Genomics Data Demonstrate Next-Generation Mapping as New Standard for Accurate and Complete Genome Assembly

Findings from 5 Posters Being Presented at ASHG 2015 Annual Meeting

SAN DIEGO, CA – October 6, 2015 – BioNano Genomics, the leader in physical genome mapping, today announced findings supporting its next-generation mapping (NGM) platform, the Irys® System, to be presented in five poster presentations at the 2015 American Society of Human Genetics (ASHG) Annual Meeting, taking place October 6 – 10, at the Baltimore Convention Center in Baltimore, Maryland.

Erik Holmlin, Ph.D., President and Chief Executive Officer of BioNano Genomics, commented, "Collective findings from these five studies further demonstrate the value of next-generation mapping, and its complementary nature to current next-generation sequencing technologies. Next-generation mapping enables researchers to obtain a full, comprehensive view of the whole genome, allowing for discoveries that were previously either very challenging or impossible with any single technology on its own. The ability to obtain critical, long-range genomic information through next-generation mapping is revolutionizing genomic research. The findings we present here at the ASHG Annual Meeting provide additional evidence that BioNano is leading the revolution."

Findings from the five studies being presented are as follows:

Poster 3118T: Mapping the "Dark Matter" of the Genome – Complex Structural Variations and Towards True Contiguity of *de novo* Assembly with Nano Channel Technology

First / Presenting Author:	Han Cao, Ph.D.
Poster Session:	Genome structure, variation and function
Date, Time:	Thursday Oct 8th, 12:00 – 1:00 p.m. ET
Location:	Exhibit Hall, Level 1

De novo physical mapping with the Irys System was applied on multiple normal and disease (cancer) human samples. Direct alignment of long raw molecules against a digitally-digested and 'barcoded' reference shows that the Irys System is able to detect haplotype differences, copy number changes, and hundreds of large structural variants. In particular, genome mapping helps reveal the locations and orientations of complex structural variants that are biologically and clinically relevant.

Rapid NGM using the Irys System represents a new standard of single-molecule platform that is independent and complementary to DNA sequencing and allows for accurate genome assembly and structural variation analysis.

Using the Irys System, researchers were able to precisely map the genomic sites associated with integration of key viral components. Integration of viral components at these sites triggers changes in the human/host genome that are believed to be linked to genome instability and oncogenesis (formation of cancer).

The system enables automated collection of high-quality data, and the study confirms that genome mapping provides a comprehensive view of the whole genome – including the unknown structural or heterozygous information, also known as the "dark matter" – via single-molecule imaging, facilitating *de novo* assembly without the guidance of a reference.

Poster 1632F: Integrated Genome Mapping in NanoChannel Arrays and Sequencing for Better Human Genome Assembly and Structural Variation Detection

First / Presenting Author:	A.W.C. Pang, Ph.D.
Poster Session:	Bioinformatics and Genomic Technology
Date, Time:	Friday Oct 9th, 11:45 a.m. – 12:45 p.m. ET
Location:	Exhibit Hall, Level 1

Results from a comprehensive analysis of a human genome that combines NGM data with one of the most completely annotated sequence assemblies, HuRef (Human Reference Genome – J. Craig Venter Institute), show that assemblies from NGM and next-generation sequencing (NGS) integrate and synergize extremely well. The resulting hybrid scaffolds are highly contiguous, with an N50 exceeding 35 Mb, a value typically unachievable by sequencing technologies alone. Results demonstrate the ability of NGM to reduce the time and cost of *de novo* assembly by using NGM and NGS together, to generate complete genome assembly.

In addition, researchers used the Irys System to compare the map-based structural variation calls with calls previously detected in the HuRef assembly and found multiple novel variants spanning hundreds of kilobases in size and encompassing numerous genes that could be functionally important. Some of these variants were found to reside in areas where the NGS assembly was poorly covered or highly fragmented. Results demonstrate the ability of NGM to accurately detect large, complex structural variants missed by short-read NGS technologies or reference-guided assembly approaches.

Poster 2721W: Towards understanding the genomic architecture of cancer genomes

First / Presenting Author:	Ernest Lam, Ph.D.
Poster Session:	Cancer Genetics
Date, Time:	Wednesday Oct 7th, 5:00 – 6:00 p.m. ET
Location:	Exhibit Hall, Level 1

Results from the study conducted in collaboration with the Eli and Edythe L. Broad Institute of MIT and Harvard, Cambridge MA, highlight the significance of NGM to discover, bridge, and potentially phase neighboring translocation events observed in well-studied cancer cell lines and multiple myeloma and prostate cancer patient tumor samples. The absence of amplification steps and its single-molecule nature make genome mapping ideal for studying clonal population structures of cancer.

The study integrated NGM using the Irys System and NGS to provide a comprehensive view of a cancer genome, enabling a more comprehensive catalogue of cancer mutations.

Overall, the study demonstrated NGM as a complementary technology to NGS providing critical long-range structural information that can be used for identifying key cancer drivers leading to the potential for enhanced diagnosis and prognosis accuracy, in addition to revealing previously unknown opportunities for targeted therapies.

Results showed that the tumor samples had highly variable copy number profiles, corresponding to focal and chromosome-scale changes and copy number breakpoints indicative of translocation events. Researchers also developed a custom analysis pipeline to integrate NGM and NGS data to validate and refine translocation calls, as well as a novel computational approach to identify translocations.

Poster 1832T: Resizing N-Base Gaps in the Human Reference Genome

First / Presenting Author:	Željko Džakula, Ph.D.

Poster Session:	Bioinformatics and Genomic Technology
Date, Time:	Thursday Oct 8th, 12:00 – 1:00 p.m. ET
Location:	Exhibit Hall, Level 1

Analysis of a large cohort of human samples highlights the utility of NGM to correctly size gaps, correct errors, and add novel information related to hg19, one of the most widely used human references. The results demonstrate the potential of NGM to greatly enhance sensitivity and specificity to detect true structural variants compared to reference errors.

Researchers used NGM with the Irys System to collect long-range genomic data and then used the resulting *de novo* assembled genome maps to estimate the sizes of the N-base gaps in the human reference. They found a high degree of consistency among the *de novo* assembled maps originating from different individuals and were able to accurately size gaps based on the population data. In certain cases, the arbitrary sizes of N-base gaps currently present in the human reference significantly differ from the population estimates. The study confirmed NGM reveals diversity among individuals, suggesting the presence of haplotypes (a set of DNA variations typically inherited together) both inside and in the vicinity of the N-base gaps.

Poster 2496F: *De Novo* Assembly of the Genome-in-a-Bottle Reference Ashkenazi Trio, Structural Variation Discovery and Comparison with Other Individuals by Genome Mapping

First / Presenting Author:	Alex Hastie, Ph.D.
Poster Session:	Cytogenetics
Date, Time:	Friday Oct 9th, 11:45 a.m. – 12:45 p.m. ET
Location:	Exhibit Hall, Level 1

The study demonstrates the ability of NGM to analyze familial trios and study common structural variants from multiple sources to establish standardized structural variation calls across multiple platforms. The study shows that NGM provides a comprehensive analysis of structural variation, thereby offering novel and indispensable information to establish a "gold standard" set of structural variation NGM calls that are unattainable with current sequencing and analysis technologies on their own.

Researchers used the Irys System to produce high resolution genome maps of Genome in a Bottle (GIAB) reference trio of Ashkenazi Jewish descent (NA24385, NA24149, NA24143) that were assembled *de novo* from single molecules to preserve long-range structural information necessary for structural variation detection. Structural variation analysis revealed insertions, deletions, inversions, including large deletions in the UGT2B17 gene (involved in graft versus host disease, osteopathic health and testosterone and estradiol levels) in the mother and son. Researchers also investigated the amylase locus in this trio as well as approximately 20 other individuals and found at least 15 different structural variants. Using NGM, researchers were also able to identify multiple copy neutral variants of human amylase genes, such as inversions, in these individuals that are often invisible to other technologies.

About Irys® System

The Irys System is BioNano Genomics' breakthrough genomics platform for genome mapping. Irys is a scalable platform that offers high quality genomic information. The system can be used for a variety of applications like structural variation analysis, next-generation sequencing (NGS) anchoring and scaffolding, and assembly validation. Irys' next-generation mapping (NGM) can provide valuable insights about the biology of the genome based on information about the order, orientation, arrangement, and interaction of genomic components. This information complements information discovered using other genomic technologies, reaching under-explored regions of the genome.

About BioNano Genomics

BioNano Genomics, Inc., the leader in next-generation mapping (NGM), provides customers with genome analysis tools that advance human, plant, and animal genomics and accelerate the development of clinical diagnostics. The Company's Irys® System uses NanoChannel arrays integrated within the IrysChip® to image genomes at the single-molecule level with average single-molecule lengths of about 350,000 base pairs, which leads the industry. The long-range genomic information obtained with the Irys System helps decipher large, complex DNA repeats, which are the primary cause of inaccurate and incomplete genome assembly.

On its own, next-generation mapping with the Irys System enables detection of structural variants, many of which have been shown to be associated with human disease as well as complex traits in plants and animals. As a companion to next-generation sequencing, next-generation mapping with the Irys System integrates with sequence assemblies to create contiguous hybrid scaffolds that reveal the highly-informative native structure of the chromosome.

Only BioNano Genomics provides long-range genomic information with the cost-efficiency and throughput to keep up with advances in next-generation sequencing.

The Irys System has been adopted by a growing number of leading institutions around the world, including: National Cancer Institute (NCI), National Institutes of Health (NIH), Wellcome Trust Sanger Institute, Broad Institute of MIT and Harvard, BGI, Garvan Institute, Salk Institute, and McDonnell Genome Institute of Washington University. Investors in the Company include Battelle Ventures, Domain Associates, Legend Capital, Novartis Venture Fund, Federated Kaufmann, Monashee Investment Management, and Gund Investment Corporation.

For more information, please visit us at www.BioNanoGenomics.com.

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