Consortium Study Finds Bionano Genomics' Optical Mapping Essential for Comprehensive Detection of Structural Variants

Most of the large SVs detected in this study's 9 human subjects by Bionano's Saphyr system were missed by Illumina and PacBio systems and other technologies. Comprehensively detecting structural variation at the root of human disease necessitates Bionano's Saphyr.

SAN DIEGO, April 17, 2019 (GLOBE NEWSWIRE) -- Bionano Genomics, Inc. (NASDAQ: BNGO), a life sciences instrumentation company that develops and markets Saphyr®, a platform for ultra-sensitive and ultra-specific structural variation detection in genome analysis and digital cytogenetics, announced the publication of a multi-platform analysis of genome structural variation by the Human Genome Structural Variation Consortium (HGSVC). The publication highlights the unique capability of Bionano's Saphyr to comprehensively detect SVs and enable the identification of their human disease associations.

A study published this week in *Nature Communications* described the results of analyzing three different trio sample sets, each comprising two parents and a child, to discover, sequence-resolve and phase (resolve the parental origin of variation in the child) all variants except single nucleotide polymorphisms (SNPs). The consortium used a suite of genome analysis tools, including the Saphyr system from Bionano, short-read sequencing from Illumina, long-read sequencing from PacBio, sample preparation and sequencing techniques like Hi-C and other tools and methods.

Genomic structural variation refers to larger sequence differences in patient samples compared to a gold standard or otherwise normal sample when studying disease populations. SVs are known to be drivers of many human diseases. For example, as much as 90% of hematologic malignancies are analyzed by evaluating large SVs or panels of large SVs. One of the best-known large SVs is the Philadelphia Chromosome, which is a translocation that causes chronic myelogenous leukemia through formation of a fusion protein. Many other fusion proteins are now therapeutic targets and the subject of ongoing clinical trials. In addition to translocations, SVs may be insertions, deletions, inversions and repeat expansions. Short-read sequencers are essentially blind to SVs larger than a few hundred base pairs (bp). The purpose of this study by the HGSVC is to reveal the wide scope of SVs in otherwise normal human genome samples and to highlight the need for solutions other than next-generation sequencing to detect them.

The study team recognized that the overall contribution of SVs to human disease has not been adequately characterized due to the genomics industry's reliance on short-read sequencing. The study claims that SVs, which remain cryptic to current sequencing methods, likely represent an important source of genomic variation in unsolved diseases involving a gene mutation.

Here, the study showed definitively that while each method detected variants within a specific window of size and type, Bionano's optical mapping uniquely excels at detecting structural variants which are 1,000 bp and larger, having no upper limit in size of variant detected. The

study showed that Illumina sequencing, by far the most commonly deployed method of genome analysis, missed 82% of all insertions, even with much higher coverage and the greater use of algorithms than is typical throughout the industry. This study also demonstrated that most larger insertions could be detected solely by Bionano. In fact, for insertions larger than 10,000 bp, Bionano detected more events than those detected by all the other genomic methods combined.

Importantly, the publication also emphasizes that high rates of inaccurate SV calling throughout the industry has made it impractical to validate all potentially disease-related SVs in human population studies. The consortium identifies a pressing need to reduce the current false positive rate of SV calling of conventional tools such as short-read and long-read sequencing. Bionano's Saphyr has the industry's lowest false positive rate for SV calling and is considered the gold standard for identifying potentially disease-related SVs. This extraordinarily low false positive rate is one of the drivers of the rapid increase in adoption of Bionano's Saphyr for both genomics research and digital cytogenetics.

Erik Holmlin, PhD, CEO of Bionano Genomics, commented: "We are pleased that the Saphyr system has been used as part of the Human Genome Structural Variation Consortium study published this week. The paper describes one of the most in-depth analyses of the structural variation of human genomes ever completed. By combining sequencing (short-read and long-read) and Bionano optical mapping, our understanding of detecting large variation of the human genome has improved. Importantly, this study clearly shows that Bionano's molecule lengths of hundreds of thousands to millions of base pairs, orders of magnitude longer than what even long-read sequencing can produce, make Bionano mapping uniquely capable of detecting large SVs. Saphyr appears to have an essential role in future comprehensive studies of genome variation for discoveries in human biology and medicine. Furthermore, now proven as the only platform capable of reliably detecting SVs greater than 10,000 bp, which is the size range where most clinically relevant SVs are found, Saphyr is poised to become the platform of choice to transform traditional cytogenetics into digital cytogenetics. We see Saphyr therefore playing a critical role in research and diagnostics."

About Bionano Genomics

Bionano is a life sciences instrumentation company in the genome analysis space. The Company develops and markets the Saphyr system, a platform for ultra-sensitive and ultra-specific structural variation detection that enables researchers and clinicians to accelerate the search for new diagnostics and therapeutic targets and to drive the adoption of digital cytogenetics, a more systematic, streamlined and industrialized form of traditional cytogenetics. The Saphyr system comprises an instrument, chip consumables, reagents and a suite of data analysis tools.

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