RESEARCH VALIDATES BIONANO GENOMICS' MAPPING PLATFORM FOR COMPLEX HUMAN GENOME ANALYSIS

Study Published in Nature Biotechnology Demonstrates Utility for Structural Variation Analysis and Sequence Assembly

SAN DIEGO—July 16, 2012—In a paper published today in *Nature Biotechnology*, researchers at the University of California San Francisco (UCSF) Institute for Human Genetics and Cardiovascular Research Institute demonstrated the utility of the Irys™ platform from BioNano Genomics for structural variation analysis and *de novo* assembly of next generation sequencing (NGS) data. Using Irys, the authors were able to accurately map and comprehensively analyze structural variation in the human major histocompatibility complex (MHC) region, which is associated with autoimmune and infectious diseases.

"While the idea of using physical genome maps has been around for some time, the methods available have not been able to accurately address complex regions in humans," said Pui-Yan Kwok, MD, PhD, senior author and Henry Bachrach Distinguished Professor at the UCSF School of Medicine. "BioNano's approach brings us one step closer to fully understanding the relevance of genetic variation in studies of new pathogens, complex metagenomics, and cancer genomes, where copy number variation and structural variation are abundant."

Complex genomes contain highly repetitive sequences and prove challenging for whole genome assembly. The MHC region is notoriously difficult to study owing to its large number of genes, repetitive sequences, extreme variation and pseudogenes. While advances have been made to short read sequencing methods attempting to address complex genomes, such methods have not performed well in repetitive regions and do not readily resolve haplotypes or localize structural variants precisely.

Irys is a multiplex-capable, scalable platform that uses a proprietary chip to uncoil and confine long DNA molecules in nanochannels, causing them to spontaneously and uniformly linearize for high-resolution, single-molecule imaging. Irys eliminates the DNA fragmentation and amplification steps typical with NGS, resulting in read lengths of hundreds of kilobases to megabases. These extremely long read lengths preserve the valuable structural information inherent in the sample, making it possible to directly observe structural variants including translocations and inversions. The system automates sample processing and imaging to provide a simple technique for genome mapping by labs of any size or level of expertise.

"The BioNano approach to genome mapping achieves uniform DNA stretching in a high throughput format, allowing researchers to directly view genome variation in the full biological context," said Dr. Erik Holmlin, CEO of BioNano Genomics. "This paper demonstrates how the Irys system provides a completely new data type that opens the door to more accurate and comprehensive structural variation discovery studies and improves our ability to achieve higher quality sequence assemblies."

Study Findings

Results showed that sequence motif maps generated by the Irys system provide useful scaffolds for *de novo* assembly of sequencing data generated from structurally complex regions for identifying misassemblies, characterization of structural variants and retention of haplotype phasing.

To demonstrate the utility of this approach, the authors constructed sequence motif maps of 95 bacterial artificial chromosome (BAC) clones covering the 4.7 Mb MHC region from two individuals (PDF and COX libraries used by the MHC Haplotype Consortium). Subsequently, they performed *de novo* sequence assembly using NGS reads. The maps and NGS contigs were then compared to the reference sequences reported by the MHC Haplotype Consortium as confirmation and to uncover potential differences.

Employing this method, the study found and confirmed a number of interesting genomic features, including a 4kb error in one reference sequence, anchoring and gap sizing of four NGS contigs, identification of misassembled NGS contigs, differentiation of the two HLA-DRB1 variants, and definition of numerous structural variants, such as a 5kb insertion and 30kb tandem duplication. The authors further concluded that the Irys is scalable to a variety of genome analyses including large-scale, whole genomes based on throughputs achieved in the study of >300 Mb per scan.

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About BioNano Genomics
Headquartered in San Diego, BioNano Genomics is delivering an altogether better way of gaining a fully informed understanding of genomes. The Company's platform provides researchers and clinicians the most comprehensive, organized and actionable picture of a genome with unprecedented insights into how the individual components of genomes are ordered, arranged, and interact with each other. BioNano Genomics works with institutions in life science, translational research, molecular diagnostics and personalized medicine. The Company is supported by private investors and grant funding from genomics programs at federal agencies, including the NIH and NIST-ATP. www.BioNanoGenomics.com

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