Highly Accurate Long-Read Sequencing of Human Genomes Leads to Discovery of Disease-Causing Variants

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Identification of pathogenic structural variants with SMRT Sequencing improves solve rate for rare and Mendelian diseases

MENLO PARK, Calif., June 13, 2019 (GLOBE NEWSWIRE) -- While DNA sequencing tools have been useful for determining the genetic cause of many diseases, there remain a large number that are left unexplained. Recently, scientists have adopted Single Molecule, Real-Time (SMRT®) Sequencing from Pacific Biosciences of California, Inc. (Nasdaq:PACB), a leading provider of high-quality sequencing of genomes, transcriptomes and epigenomes, to study previously unsolved diseases. Many high-impact research publications report expanded variant detection in human genomes, leading to discovery of disease-causing variants and genes underlying rare and Mendelian disorders.

In a *Nature Communications* publication, scientists report that most structural variants (SVs) and large indels are undetected in today's human genetic studies, which likely accounts for some of the missing heritability of genetic disease[1]. Meanwhile, several studies have demonstrated that these missing variants can be discovered routinely using highly accurate long reads (HiFi reads) generated by the PacBio® Sequel II® System[2,3]. A review article from scientists at Radboud University Medical Center summarizes many of these findings, including genetic discovery results for ALS, Huntington's disease, Parkinsonism, epilepsy, ataxias, myotonic dystrophy, and Fragile X disorders [4].

For example, scientists in Japan turned to SMRT Sequencing to explain a familial form of epilepsy that had not been solved with whole exome sequencing. PacBio whole genome sequencing data allowed the team to detect more than 17,000 SVs and quickly identify the 12.4 kb deletion responsible for the family's condition [5]. The team determined that "long-read sequencing ensures unbiased coverage even in GC-rich repetitive sequences, which enables the identification of previously unidentified pathogenic SVs."

"Far too many genetic diseases have gone unsolved in the genomic era, and it's becoming clear that some of the answers were simply not conducive to detection with previous technologies," said Jonas Korlach, Chief Scientific Officer of Pacific Biosciences. "It's been tremendously gratifying to see the flurry of recent publications reporting the discovery of underlying causes for some of these diseases through the use of SMRT Sequencing systems."

Additional studies describing novel disease-causing variant detection with SMRT Sequencing will be presented at the European Society of Human Genetics (ESHG) 2019 Annual Meeting, taking place June 15-18 in Gothenburg, Sweden. To learn more, please visit PacBio in ESHG booth #560 or download a flyer with a list of featured presentations at: https://www.pacb.com/wp-content/uploads/2019-ESHG-Program-Flyer.pdf.

References

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About Pacific Biosciences

Pacific Biosciences of California, Inc. (NASDAQ:PACB) offers sequencing systems to help scientists resolve genetically complex problems. Based on its novel Single Molecule, Real-Time (SMRT®) technology, Pacific Biosciences' products enable: *de novo* genome assembly to finish genomes in order to more fully identify, annotate and decipher genomic structures; full-length transcript analysis to improve annotations in reference genomes, characterize alternatively spliced isoforms in important gene families, and find novel genes; targeted sequencing to more comprehensively characterize genetic variations; and real-time kinetic information for epigenome characterization. Pacific Biosciences' technology provides high accuracy, ultra-long reads, uniform coverage, and the ability to simultaneously detect epigenetic changes. PacBio® sequencing systems, including consumables and software, provide a simple, fast, end-to-end workflow for SMRT Sequencing. More information is available at www.pacb.com.

Forward-Looking Statements

All statements in this press release that are not historical are forward-looking statements, including, among other things, statements relating to the attributes of the Sequel II System, the future availability, uses, accuracy, quality or performance of, or benefits of using, products or technologies, the suitability or utility of methods, products or technologies for particular applications, studies or projects, the importance of long-read sequencing data, the expected benefits of sequencing projects, and other future events. You should not place undue reliance on forward-looking statements because

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