Pacific Biosciences Contributes Whole Genome Sequence Data for German E. Coli Outbreak Strain and 11 Related Strains for Comparative Analysis

Improved Chemistry and Software Provides Higher Accuracy Single Molecule Reads and Longer Readlengths to Yield PacBio-only De Novo Assembly

MENLO PARK, Calif.--(BUSINESS WIRE)-- Pacific Biosciences of California, Inc. (NASDAQ: PACB) announced that it has completed a *de novo* sequence assembly of the *Escherichia coli* O104:H4 strain responsible for the recent outbreak in Germany using its Single Molecule Real Time (SMRT™) technology, and sequenced 11 related bacterial strains (including six previously unsequenced strains of the same serotype) for comparative analyses. An international team of scientific experts on *E. coli* collaborated on the rapid sequencing project to provide more comprehensive information about the origins of the strain that gave rise to the deadly outbreak. The data were generated using an early version of chemistry and software in development at Pacific Biosciences for the next major PacBio *RS* product upgrade, planned for the fourth quarter of 2011.

The data provided to the public domain includes a complete assembly of the German outbreak strain, alignment to assemblies from other outbreak isolates, and sequences for 11 related Enteroaggregative *E. coli* strains. The project demonstrates the ability to produce a PacBio-only *de novo* assembly for a complex microbial pathogen, and the power of rapid sequencing of multiple genomes with the PacBio *RS* to elucidate the evolutionary history of a pathogenic microbe. A summary of the project appears on the company's website at http://blog.pacificbiosciences.com.

The Pacific Biosciences scientific team, led by Chief Scientific Officer Eric Schadt, Ph.D., is collaborating with some of the world's leading experts on *E. coli* and infectious diseases for this project. The collaborators include:

In Europe:

- Karen Angeliki Krogfelt, Ph.D., Professor, Head of Unit, Gastrointestinal Infections, Statens Serum Institut (SSI), Denmark
- Flemming Scheutz, Ph.D., Head of the WHO Collaborating Centre for Reference and Research on *Escherichia* and *Klebsiella*, SSI, Denmark

In the U.S.:

- James P. Nataro, M.D., Ph.D., Professor and Chair, Pediatrics, University of Virginia School of Medicine
- David A. Rasko, Ph.D., Assistant Professor, University of Maryland School of Medicine, Institute for Genome Sciences and Department of Microbiology and Immunology
- Nadia Boisen, Ph.D., Research Scientist, Department of Pediatrics, University of Virginia School of Medicine
- Matthew K. Waldor, M.D., Ph.D., Professor of Medicine at Harvard Medical School, Brigham and Women's Hospital, and HMMI

"Using samples provided by our collaborators, we rapidly sequenced each strain using a standard PacBio *RS* protocol that took on average less than eight hours from sample preparation to sequencing results," said Dr. Schadt. "The ability to sequence the outbreak strain with reads averaging 2,900 base pairs and our longest reads at over 7,800 bases, combined with our circular consensus sequencing to achieve high single molecule accuracy with a mode accuracy distribution of 99.9%, enabled us to complete a PacBio-only assembly without having to construct specialized fosmid libraries, perform PCR off the ends of contigs, or other such techniques that are required to get to similar assemblies with second generation DNA sequencing technologies."

Dr. Krogfelt commented: "These high quality data will provide scientists with more information about the genomic features of this strain that could provide new markers for predicting the higher degree of pathogenicity we are seeing with this outbreak. A more comprehensive evolutionary view of this pathogen may also help identify markers for antibiotic drug resistance that could be used in the future should other related strains emerge. The complexity of this case proves that international collaborations and communications are important in the achievement of detailed scientific information."

The data are available for the bioinformatics community at the PacBio developer's network (DevNet) web site (www.pacbiodevnet.com), where a suite of open source tools and other resources designed for SMRT sequence data are available to analyze the information. The data have also been submitted to the National Center for Biotechnology Information (NCBI) SRA database.

While not involved with the current *E. Coli* study, the Broad Institute has been testing the new version of the sequencing enzyme in development as part of Pacific Biosciences' early access program. "We are seeing significant increases in readlength, with high quality runs producing reads with average 2,000 base readlengths or more," said Chad Nusbaum, co-director of the Genome Sequencing and Analysis program at the Broad Institute. "The potential for even greater readlengths and the possibility to trade off readlength to increase accuracy will be important for bringing the PacBio *RS* to an increasing application space. We have been impressed with the rapid progress PacBio has made in improving their technology in a relatively short amount of time."

Hugh Martin, Chairman and CEO of Pacific Biosciences stated: "Since this collaboration employed an early version of our chemistry and software in development for the next major upgrade of our product, we are taking this opportunity to share some of the specifications that we expect to reach for that planned Q4 upgrade. As demonstrated by the *E. coli* project, we are already seeing a big step up from the specifications for the first commercial release in April, and we expect to achieve even more significant performance increases." While not yet fully optimized, the specifications are based on flexible parameters with the capability to produce:

- An average of 2,700 base pair reads, with 5% of the reads achieving 5,100+ base pairs
- Up to 90 megabases of mappable data per SMRT Cell
- 1,350 base pair reads with 2X circular consensus sequencing single molecule accuracy of 93%

For more information about Pacific Biosciences, please visit www.pacificbiosciences.com. You can also follow the company on twitter www.twitter.com/pacbio.

About Pacific Biosciences

Pacific Biosciences' mission is to transform the way humankind acquires, processes and interprets data from living systems through the design, development and commercialization of innovative tools for biological research. The company has developed a novel approach to studying the synthesis and regulation of DNA, RNA and proteins. Combining recent advances in nanofabrication, biochemistry, molecular biology, surface chemistry and optics, Pacific Biosciences has created a powerful technology platform called single molecule, real-time, or SMRT™, technology. SMRT technology enables real-time analysis of biomolecules with single molecule resolution, which has the potential to transform the understanding of biological systems by providing a window into these systems that has not previously been open for scientific study.

Forward-Looking Statements

This press release contains forward-looking statements. Forward-looking statements may contain words such as "believe," "may," "estimate," "anticipate," "continue," "intend," "expect," "plan," the negative of these terms, or other similar expressions, and include the assumptions that underlie such statements. Such statements include, but are not limited to, statements regarding the Company's SMRT technology. These statements are subject to known and unknown risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements, including but not limited to risks discussed from time to time in documents Pacific Biosciences of California, Inc. has filed with the Securities and Exchange Commission, including the risks identified under the section captioned "Risk Factors" in its recently filed Quarterly Report on Form 10-Q. All forward-looking statements are based on estimates, projections and assumptions as of the date hereof. Pacific Biosciences undertakes no obligation to update any forward-looking statements.

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