

## Pacific Biosciences and Harvard Scientists Decode Genome of Haitian Cholera Pathogen

*Rapid Whole Genome Sequencing and Analysis of Five V. Cholerae Strains Supports South Asian Lineage; Sets Groundwork for Potential New Preventative or Therapeutic Strategies*

MENLO PARK, Calif.--(BUSINESS WIRE)-- Scientists from Pacific Biosciences of California, Inc. (NASDAQ:PACB) and Harvard Medical School have successfully employed single molecule, real-time (SMRT™) DNA sequencing technology to rapidly characterize the pathogen responsible for the recent deadly cholera epidemic in Haiti. Published online Thursday in the *New England Journal of Medicine*, the results provide the first whole genome sequence analysis and most detailed genetic profile to date of the Haitian *Vibrio cholerae* outbreak strain.

The multi-strain sequencing and bioinformatic analysis confirm that the cholera pathogen now present in Haiti is closely related to the "El Tor O1" variant from South Asia. Given that the existence of this strain has never been documented in the Caribbean region or throughout Latin America, the evidence suggests that the Haitian epidemic began as a result of the introduction of a new strain from a distant geographic source. While the sequence analysis confirms a South Asian lineage, it does not identify the specific source of the Haitian strain or suggest how it may have arrived in the country.

In this collaboration, DNA prepared from five *V. cholerae* strains at Harvard Medical School was received at Pacific Biosciences on Wednesday, November 10, 2010. "Through the truly remarkable and dedicated efforts of Dr. Schadt and his colleagues at PacBio, we had a good understanding of the genome of the Haitian *V. cholerae* isolates and their likely origin by Friday evening, November 12," said John Mekalanos, Ph.D., Chair of the Department of Microbiology and Molecular Genetics at Harvard Medical School, a senior author on the study. "This understanding has important public health policy implications for preventing cholera outbreaks in the future."

Members of a team led by Stephen Calderwood, M.D., Chief of the Division of Infectious Diseases at Massachusetts General Hospital and Morton N. Swartz M.D. Academy Professor of Medicine (Microbiology and Molecular Genetics) at Harvard Medical School, recently returned from working alongside public health experts in Haiti where they collected samples for the study in cooperation with Haitian collaborators.

"Witnessing the scale of human suffering caused by the rapidly progressing cholera outbreak, our team was compelled to deploy a technology that could immediately provide comprehensive genomic information about this virulent strain and quickly get it into the hands of the global health and research community," said Jason Harris, M.D., Physician, Pediatric Infectious Disease Unit at Massachusetts General Hospital and Assistant Professor of Pediatrics at Harvard Medical School. "In the initial stages of a major epidemic, real time is the speed we need to be working in order to have the greatest impact on saving lives."

Whole genome sequencing involves decoding the precise order of nucleotide bases that make up an organism's complete set of DNA and provides more comprehensive information than other analysis methods such as DNA fingerprinting or arrays. With advances in technology and decreasing cost, whole genome sequencing is emerging as the gold standard method for identifying and classifying infectious agents. SMRT technology is the latest advance in DNA sequencing, capable of generating long sequence reads to resolve structural variations and complex genomes at ultra-fast speeds by 'eavesdropping' on DNA replicating in real time.

"Now armed with a more complete characterization of this pathogen, the scientific community is empowered with information that can be used to inform public health policy decisions such as the appropriate use of vaccines to quell this epidemic," said Eric Schadt, Ph.D., Chief Scientific Officer of Pacific Biosciences and co-author of the paper. "The ability to quickly and easily perform real-time monitoring of pathogens also opens the door to using this technology as a routine surveillance method, for public health protection in addition to pandemic prevention and response."

To obtain a comprehensive genomic characterization of the origin of the Haitian cholera pathogen, the PacBio/Harvard team sequenced two samples from the current Haiti outbreak, two samples from South Asia (Bangladeshi isolates from 1971 and 2008), and one sample from Latin America (a 1991 Peruvian isolate). The team then compared this high resolution whole genome sequence information to DNA sequence information available in public databases for 23 diverse strains of *V. cholerae*.

Matthew Waldor, M.D., Ph.D., Professor of Medicine at Harvard Medical School, and Howard Hughes Medical Institute Investigator, is the lead author on the paper entitled "The Origin of the Haitian Cholera Outbreak Strain." A copy of the paper is available at [www.nejm.com](http://www.nejm.com).

Real-time infectious disease monitoring is featured in a new documentary film that was produced by Pacific Biosciences called

"The New Biology." The film profiles how new technologies are leading to advances in cancer, infectious diseases, and agriculture. To view the infectious disease segment, visit <http://www.pacificbiosciences.com/newbio>.

More information about SMRT technology is available at [www.pacificbiosciences.com](http://www.pacificbiosciences.com).

## **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.

This press release contains forward-looking statements, including statements regarding our belief that our SMRT technology could be used as a routine surveillance method for public health protection in addition to pandemic prevention or response, and our expectation that the ability to rapidly access complete sequence information for bacterial or viral pathogens will greatly improve the identification and surveillance of infectious diseases, as well as provide a more complete characterization of medically relevant molecular targets for potential new vaccines or therapeutics. Forward-looking statements may contain words such as "believe," "will," "may," "estimate," "anticipate," "continue," "intend," "expect," "plan," the negative of these terms, or other similar expressions, and include the assumptions that underlie such statements. 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 we have filed with the Securities and Exchange Commission, including the risks identified under the section captioned "Risk Factors" in our final prospectus relating to our initial public offering filed pursuant to Rule 424(b) under the Securities Act of 1933, as amended, on October 27, 2010. All forward-looking statements are based on management's estimates, projections and assumptions as of the date hereof. We undertake no obligation to update any forward-looking statements.

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