PacBio Announces Plans to Improve Methylation Detection in HiFi Chemistry

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Company licenses novel deep learning-based epigenetic models from CUHK enabling the detection of 5hmC, 5mC hemimethylation, and 6mA in standard sequencing runs

MENLO PARK, Calif., April 28, 2025 (GLOBE NEWSWIRE) -- PacBio (Nasdaq: PACB), a leading provider of high-quality, highly accurate sequencing platforms, today announced it plans to improve on its already highly accurate methylation detection capabilities in HiFi chemistry through licensing advanced DNA methylation detection methods developed by Professor Dennis Lo and colleagues at the The Chinese University of Hong Kong (CUHK) and Centre for Novostics. The licensed technology is designed to enhance PacBio HiFi sequencing with improved detection of DNA base modifications—including 5-hydroxymethylcytosine (5hmC) and hemimethylated 5-methylcytosine (5mC)—in native DNA. PacBio plans to bring these capabilities to its Revio and Vega systems, building on its existing 5mC support to deliver even more comprehensive epigenomic insights as part of standard HiFi whole-genome sequencing workflows.

“PacBio was the first to detect native epigenetic modifications alongside accurate DNA sequencing. With the integration of the CUHK deep learning models, our technology will be able to detect many additional and biologically meaningful methylation signatures, including 5hmC and strand-specific 5mC,” said Christian Henry, President and CEO of PacBio. "Our commitment to continually improving HiFi chemistry will enable our customers to gain even deeper insights into the human genome, powering new discoveries and clinical possibilities."

The newly licensed technology includes an enhanced AI deep learning framework known as Holistic Kinetic Model 2 (HK2), which integrates convolutional and transformer layers to model local and long-range kinetic features with extraordinary precision. HK2 is designed to significantly improve the accuracy of 5mC and N6-methyladenine (6mA) detection and introduces native 5hmC calling in single molecules—a first for HiFi sequencing.

HiFi sequencing, available on both the Revio and Vega platforms, provides a comprehensive and simultaneous readout of the genome and epigenome from native DNA without the need for chemical conversion, additional sample preparation, or parallel workflows. The new capabilities from the HK2 model will be delivered to existing customers through software updates, with no changes to sequencing protocols and no additional cost.

“I am delighted to see this technology now being deployed more broadly through PacBio’s global customer base,” said Professor Dennis Lo, Scientific Director of Centre for Novostics, CUHK. “Accurate detection of DNA methylation—particularly 5mC and 5hmC—on native molecules is important for advancing research in cancer, human development, and beyond. With the improvements enabled by HK2, methylation calling with PacBio HiFi sequencing is poised to set a new standard for accuracy in the industry, surpassing other available technologies.”

CUHK, together with Take2 Technologies Limited, a Hong Kong-based biotechnology company, pioneered robust 5mC detection in 2021 using the PacBio platform. PacBio introduced on-instrument 5mC detection in April 2022 and extended support to 6mA in December 2024 for Fiber-seq chromatin architecture studies. HK2 is designed to push detection performance to new levels of accuracy. Importantly, HK2 will also enable strand-specific 5mC analysis, which opens new opportunities to study hemimethylation—an emerging epigenetic signal.

HiFi 5-base sequencing has already been adopted by pioneering institutions such as Children’s Mercy Kansas City, the first to use comprehensive genomic and epigenomic profiling in a clinical setting. GeneDx is also leveraging this capability to investigate the diagnostic potential of epigenetic signals in neonatal care.

The ability to profile 5hmC—a dynamic and tissue-specific epigenetic mark implicated in brain development, cancer, and neurodegenerative diseases—opens new frontiers in liquid biopsy, cancer detection, and cell-free DNA analysis. Unlike chemical-based methods such as bisulfite or TAPS sequencing, which degrade DNA and diminish phasing and structural context, PacBio’s native detection maintains DNA integrity and supports haplotype-resolved analysis in complex genomic regions.

The licensing of HK2 marks another milestone in PacBio’s continued leadership in long-read epigenomics. Combined with the high accuracy and long read lengths of HiFi sequencing, HK2 delivers a uniquely powerful tool for understanding the full landscape of genome function—across both sequence and modification.

"By enabling high-resolution, native detection of 5mC, 6mA, and 5hmC, we’re empowering researchers to ask more sophisticated questions and uncover new biology," said Mark Van Oene, Chief Operating Officer at PacBio. "And because this capability is powered entirely by software and existing sequencing signals, customers can access it with no added cost or workflow changes."

PacBio aims to deliver these capabilities to Revio and Vega through a future software update. For more information about HiFi chemistry, visit https://www.pacb.com/technology/hifi-sequencing/.

About Pacific Biosciences
PacBio (NASDAQ: PACB) is a premier life science technology company that designs, develops, and manufactures advanced sequencing solutions to help scientists and clinical researchers resolve genetically complex problems. Our products and technologies stem from two highly differentiated core technologies focused on accuracy, quality and completeness which include our HiFi long-read sequencing and our SBB® short-read sequencing technologies. Our products address solutions across a broad set of research applications including human germline sequencing, plant and animal sciences, infectious disease and microbiology, oncology, and other emerging applications. For more information, please visit www.pacb.com and follow @PacBio.

PacBio products are provided for Research Use Only. Not for use in diagnostic procedures.

About The Chinese University of Hong Kong (CUHK)

Founded in 1963, CUHK is a leading comprehensive research university with a global reputation and world-leading rankings. Located in the heart of Asia, CUHK has a vision and a mission to combine tradition with modernity, and to bring together China and the West. The University is devoted in cutting edge research and translation of research outputs into useful products. CUHK is renowned for its leading role in molecular diagnostics research. The noninvasive prenatal diagnostic test for Down syndrome developed by Dennis Lo is widely adopted globally with more than 100 million tests performed since its inception. Centre for Novostics, an affiliate CUHK, is supported by the InnoHK initiative under the Innovation and Technology Commission of the Hong Kong Special Administrative Region Government dedicated to molecular diagnostic research.

About Take2 Technology Limited (Take2)
Founded in 2019, Take2 is a Hong Kong-based biotechnology company. Take2 focuses on the development of novel molecular diagnostic approaches, in particular in the area of epigenetic analysis and cancer screening.

Forward Looking Statements
This press release contains “forward-looking statements” within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and the U.S. Private Securities Litigation Reform Act of 1995. All statements other than statements of historical fact are forward-looking statements, including statements relating to the uses, advantages, quality or performance of, the benefits or expected benefits of using, PacBio products or technologies, including in connection with anticipated improvements to methylation detection with respect to 5hmC, 5mC, 6mA, and strand-specific 5mC, and related opportunities for customers to gain deeper insights, power new discoveries and enable clinical possibilities with no additional cost or change to sequencing protocols; setting new standards for accuracy, and other future events. You should not place undue reliance on forward-looking statements because they are subject to assumptions, risks, and uncertainties that could cause actual outcomes and results to differ materially from currently anticipated results. These risks include, but are not limited to, risks inherent in developing and commercializing new technologies; rapidly changing technologies and extensive competition in genomic sequencing; unanticipated increases in costs or expenses; interruptions or delays in the supply of components or materials for, or manufacturing of, PacBio products and products under development; third-party claims alleging infringement of patents and proprietary rights or seeking to invalidate PacBio's patents or proprietary rights; and other risks associated with general macroeconomic conditions and geopolitical instability. Additional factors that could materially affect actual results can be found in PacBio's most recent filings with the Securities and Exchange Commission, including PacBio's most recent reports on Forms 8-K, 10-K, and 10-Q, and include those listed under the caption “Risk Factors.” These forward-looking statements, including PacBio’s preliminary unaudited financial information and PacBio’s financial guidance, are based on current expectations and speak only as of the date hereof; except as required by law, PacBio disclaims any obligation to revise or update these forward-looking statements to reflect events or circumstances in the future, even if new information becomes available.

Contacts

Investors:
Todd Friedman
ir@pacificbiosciences.com

Media:
pr@pacificbiosciences.com