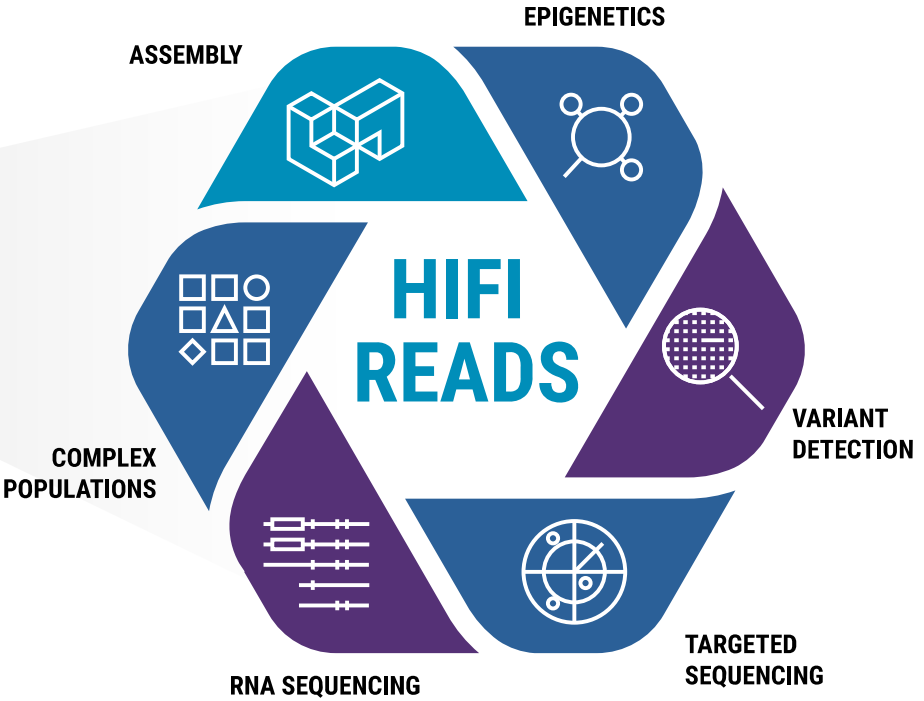
PACBIO®

HIFI SEQUENCING:
SEE WHAT YOU'VE BEEN MISSING

Dr. Jennifer L Stone, VP Segment Marketing

All statements in this presentation that are not historical are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements generally relate to future events or our future financial or operating performance and are based on management's current beliefs, assumptions and projections and on information available to management as of the date of this presentation. Forward-looking statements include, among other things, statements regarding opportunities for impact in human genetics with Company products and technology, including markets involving rare disease, pharmacogenomics, neurological disorders, cancer, reproductive issues and organ/tissue transplants; potential impact on genomics, including the ability to provide to and support customers with both long-read and short-read sequencing technologies, the accuracy of SBB sequencing, partnership opportunities and potential synergies associated with the merger of Omniome and Pacific Biosciences; and potential new advancements to workflows, including any related benefits, attributes and expected launch dates in connection therewith. Accordingly, you should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, changes in circumstances and other factors that are, in some cases, beyond the Company's control and could cause actual results to differ materially from the information expressed or implied by forward-looking statements made in the presentation. Factors that could materially affect actual results can be found in our filings with the Securities and Exchange Commission, including our most recent reports on Forms 8-K, 10-K and 10-Q, and include those listed under the caption "Risk Factors." The Company undertakes no obligation to revise or update information in this presentation to reflect events or circumstances in the future, even if new information becomes available.

COMPLETE + ACCURATE LONG-READ SEQUENCING ENABLES MULTIPLE APPLICATIONS



“PACBIO [HIFI] PROVIDES THE LOWEST ERROR RATE OUT OF ALL TECHNOLOGIES.”

nature biotechnology

Article | Published: 09 September 2021

Performance assessment of DNA sequencing platforms in the ABRF Next-Generation Sequencing Study

Jonathan Foox , Scott W. Tighe , […] Christopher E. Mason

Nature Biotechnology 39 , 1129–1140 (2021)

Abstract

Assessing the reproducibility, accuracy and utility of massively parallel DNA sequencing platforms remains an ongoing challenge. Here the Association of Biomolecular Resource Facilities (ABRF) Next-Generation Sequencing Study ben hmarks the performance of a set of sequencing nstruments (HiSeq/ aSeq/paired-

“PacBio [HIFI] had the highest reference-based mapping rate and lowest non-mapping rate.”

“Within both homopolymer and STR classes, PacBio [HIFI] showed the lowest mismatch rate.”

“PacBio [HIFI] achieved the highest precision [in accessing variants in clinically relevant regions].”

Performance benchmark of Illumina HiSeq/NovaSeq | Ion S5/Proton | PacBio Sequel II
ONT PromethION/MinION/Flongle | BGISEQ-500/MGISEQ-2000 | GenapSys GS111

https://www.nature.com/articles/s41587-021-01049-5

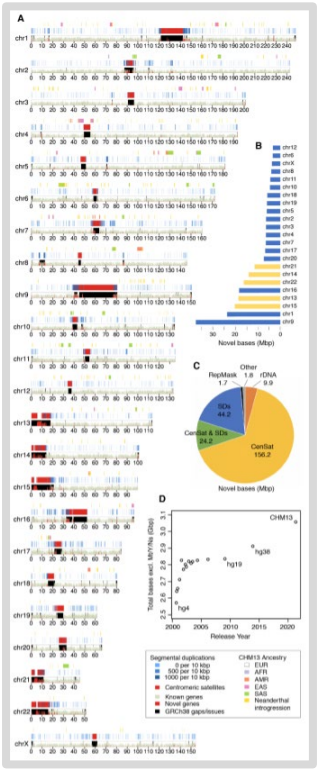
AFTER 20 YEARS… FINALLY, A COMPLETE HUMAN REFERENCE

Telomere-To-telomere Consortium

The complete sequence of a human genome

Sergey Nurk[1,*], Sergey Koren[1,*], Arang Rhie[1,*], Mikko Rautiainen[1,*], Andrey V. Bzikadze[2], Alla Mikheenko[3], Mitchell R. Vollger[4], Nicolas Altemose[5], Lev Uralsky[6,7], Ariel Gershman[8], Sergey Aganezov[9], Savannah J. Hoyt[10], Mark Diekhans[11], Glennis A. Logsdon[4], Michael Alonge[9], Stylianos E. Antonarakis[12], Matthew Borchers[13], Gerard G. Bouffard[14], Shelise Y. Brooks[14], Gina V. Cal… Richard Durbin[21], Tatiana Dvorkina[3], … Chin[18], William Chow[19], Leonardo G. de Lima[13], Philip C. Dishuck… Ian T. Fiddes[22], Giulio Formenti[23,24], Robert S. Fulton[25], Arkaracha… Patrick G.S. Grady[10], Tina A. Graves-Lindsay[27], Ira M. Hall[28], Nan… Marina Haukness[11], Kerstin Howe[19], Michael W. Hunkapiller[30], Chi… Jarvis[23,24], Peter Kerpedjiev[32], Melanie Kirsche[9], Mikhail Kolmogor… Heng Li[16,17], Valerie V. Maduro[34], Tobias Marschall[35], Ann M. McC… Miller[4,37], James C. Mullikin[14,29], Eugene W. Myers[38], Nathan D. Ol… Pavel A. Pevzner[33], David Porubsky[4], Tamara Potapova[13], Evgeny… Steven L. Salzberg[9,42], Valerie A. Schneider[43], Fritz J. Sedlazeck[44], Alaina Shumate[42], Yumi Sims[19], Arian F. A. Smit[45], Daniela C. Sot… Aaron Streets[5,47], Beth A. Sullivan[48], Françoise Thibaud-Nissen[43], … Brian P. Walenz[1], Aaron Wenger[30], Jonathan M. D. Wood[19], Chuni… Young[14], Samantha Zarate[9], Urvashi Surti[50], Rajiv C. McCoy[49], Me… Jennifer L. Gerton[13], Rachel J. O'Neill[10], Winston Timp[8,42], Justi… Eichler[4,24,†], Karen H. Miga[11,†], Adam M. … lippy[1,†]

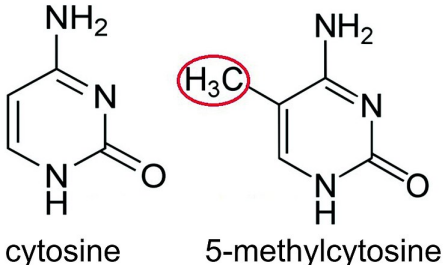
"This 8% of the genome has not been overlooked due to its lack of importance, but rather due to technological limitations… High-accuracy long-read sequencing has finally removed this technological barrier, enabling comprehensive studies of genomic variation across the entire human genome."



https://www.biorxiv.org/content/10.1101/2021.05.26.445798v1

PACBIO IS ENABLING DISCOVERY…

EPIGENETICS



cytosine 5-methylcytosine

Genome-wide detection of cytosine methylation by single molecule real-time sequencing

O Y Olivia Tse [1 2], Peiyong Jiang [1 2], Suk Hang Cheng [1 2], Wenlei Peng [1 2], Huimin Shang [1 2], John Wong [3], Stephen L Chan [4 5], Liona C Y Poon [6], Tak Y Leung [6], K C Allen Chan [1 2 5], Rossa W K Chiu [1 2], Y M Dennis Lo [7 2 5]

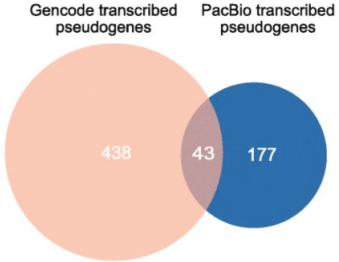
Affiliations + expand

PMID: 33495335 PMCID: PMC7865158 DOI: 10.1073/pnas.2019768118

Abstract

5-Methylcytosine (5mC) is an important type of epigenetic modification. Bisulfite sequencing (BS-seq) has limitations, such as severe DNA degradation. Using single molecule real-time sequencing, we developed a methodology to directly examine 5mC. This approach holistically examined kinetic signals of a DNA polymerase (including interpulse duration and pulse width) and sequence context for every nucleotide within a measurement window, termed the holistic kinetic (HK) model. The measurement window of each analyzed double-stranded DN… ecule comprised 21 nucleotides with a cytosine … CpG site in the cen… We used … …

FUNCTIONAL PSEUDOGENE IDENTIFICATION



Long-read cDNA sequencing identifies functional pseudogenes in the human transcriptome

Robin-Lee Troskie [1], Yohaann Jafrani [1], Tim R Mercer [2], Adam D Ewing [3], Geoffrey J Faulkner [4 5], Seth W Cheetham [6]

Affiliations + expand

PMID: 33971925 PMCID: PMC8108447 DOI: 10.1186/s13059-021-02369-0

Abstract

Pseudogenes are gene copies presumed to mainly be functionless relics of evolution due to acquired deleterious mutations or transcriptional silencing. Using deep full-length PacBio cDNA sequencing of normal human tissues and cancer cell lines, we identify here hundreds of novel transcribed pseudogenes expressed in tissue-specific patterns. Some pseudogene transcripts have intact open reading frames and are translated in cultured cells, representing unannotated protein-coding genes. To assess th… biological impa… …ding pseu… …es, we CR… …

FULL-LENGTH TRANSCRIPTS: BULK OR SINGLE-CELL

Mapping and modeling the genomic basis of differential RNA isoform expression at single-cell resolution with LR-Split-seq

Elisabeth Rebboah, Fairlie Reese, Katherine Williams, Gabriela Balderrama-Gutierrez, Cassandra McGill, Diane Trout, Isaryhia Rodriguez, Heidi Liang, Barbara J. Wold, Ali Mortazavi

doi: https://doi.org/10.1101/2021.04.26.441522

Abstract

Alternative RNA isoforms are defined by promoter choice, alternative splicing, and polyA site selection. Although… eukaryotes, it has… the uncertainties i… The rise in through… principle, to unam… its application to s… develop and …

A single-cell survey of cellular hierarchy in acute myeloid leukemia

Junqing Wu [1 2], Yanyu Xiao [1 2], Jie Sun [3], Huiyu Sun [1 2], Haide Chen [1 2], Yuanyuan Zhu [3], Huarui Fu [3], Chengxuan Yu [1 2], Weigao E [1 2], Shujing Lai [1 2], Lifeng Ma [1 2], Jiaqi Li [1 2], Lijiang Fei [1 2], Mengmeng Jiang [1 2], Jingjing Wang [1 2], Fang Ye [1 2], Renying Wang [1 2], Ziming Zhou [1 2], Guodong Zhang [1 2], Tingyue Zhang [1 2], Qiong Ding [4], Zou Wang [4], Sheng Hao [4], Lizhen Liu [3], Weiyan Zheng [3], Jingsong He [3], Weijia Huang [3], Yungui Wang [5], Jin Xie [6], Tiefeng Li [7], Tao Cheng [8 9], Xiaoping Han [10 11 12], He Huang [13 14 15 16 17], Guoji Guo [18 19 20 21 22]

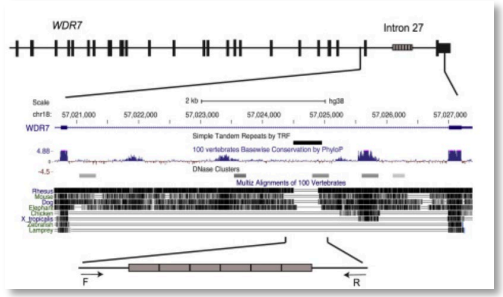
PMID: 32977829 PMCID: PMC7517826 DOI: 10.1186/s13045-020-00941-y

Abstract

Background: Acute myeloid leukemia (AML) is a fatal hematopoietic malignancy and has a prognosis that varies with its genetic complexity. However, there has been no appropriate integrative analysis on the hierarchy of …ferent AML sub…

PACBIO IS ENABLING DISCOVERY… AND TRANSLATIONAL IMPACT

REPEAT EXPANSION DISORDERS



Evolution of a Human-Specific Tandem Repeat Associated with ALS

Meredith M Course [1], Kathryn Gudsnuk [1], Samuel N Smukowski [1], Kosuke Winston [1], Nitin Desai [1], Jay P Ross [2], Arvis Sulovari [3], Cynthia V Bourassa [4], Dan Spiegelman [4], Julien Couthouis [5], Chang-En Yu [6], Debby W Tsuang [6], Suman Jayadev [7], Mark A Kay [8], Aaron D Gitler [5], Nicolas Dupre [9], Evan E Eichler [10], Patrick A Dion [4], Guy A Rouleau [11], Paul N Valdmanis [12]

PMID: 32750315 PMCID: PMC7477013 DOI: 10.1016/j.ajhg.2020.07.004

Abstract

Tandem repeats are proposed to contribute to human-specific traits, and more than 40 tandem repeat expansions are known to cause neurological disease. Here, we characterize a human-specific 69 bp variable number tandem repeat (VNTR) in the last intron of WDR7, which exhibits striking variability in both copy number and nucleotide [illegible]sition, as revealed by long-read sequencing [illegible]dition, greater

INFANTILE SUDDEN DEATH

Long-read sequencing identified a novel nonsense and a de novo missense of PPA2 in trans in a Chinese patient with autosomal recessive infantile sudden cardiac failure

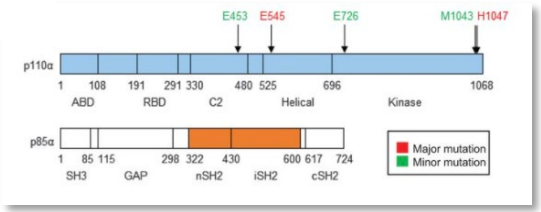
Arman Zhao [1], Jie Shen [2], Yueyue Ding [3], Mao Sheng [4], Mengying Zuo [5], Haitao Lv [6], Jian Wang [7], Yiping Shen [8], Hongying Wang [9], Ling Sun [10]

PMID: 33826954 DOI: 10.1016/j.cca.2021.03.029

Abstract

Background and aims: Biallelic missense variants in PPA2 gene cause infantile sudden cardiac failure (SCFI; OMIM #617222) characterized by sudden cardiac failure, sudden cardiac death in infants. Here, we present an unusual survivor with one inherited plus one de novo variant in PPA2. Since next-generation sequencing (NGS) fails to resolv[illegible]t phasing, which require long-read sequencing [illegible]rify the diagnosi

THERAPEUTIC RESPONSE



Double PIK3CA mutations in cis increase oncogenicity and sensitivity to PI3CAα inhibitors

Neil Vasan [1 2 3], Pedram Razavi [# 1 2], Jared L Johnson [# 3], Hong Shao [# 1], Hardik Shah [4], Alesia Antoine [4], Erik Ladewig [1], Alexander Gorelick [1 5], Ting-Yu Lin [3], Eneda Toska [1], Guotai Xu [1], Abiha Kazmi [1], Matthew T Chang [6], Barry S Taylor [1 5 7], Maura N Dickler [2 8], Komal Jhaveri [2], Sarat Chandarlapaty [1 2], Raul Rabadan [9], Ed Reznik [5 7], Melissa L Smith [4 10], Robert Sebra [4 10 11], Frauke Schimmoller [6], Timothy R Wilson [6], Lori S Friedman [12], Lewis C Cantley [3], Maurizio Scaltriti [13 14], José Baselga [13 2]

PMID: 31699932 PMCID: PMC7173400 DOI: 10.1126/science.aaw9032

Abstract

Activating mutations in PIK3CA are frequent in human breast cancer, and phosphoinositide 3-kinase alpha (PI3K α) inhibitors have been approved for therapy. To characterize determinants of sensitivity to these agents, we analyzed PIK3CA-mutant cancer genomes and observed the presence of multiple PIK3CA mutations in 12 to 15% of br[illegible]east cancers and other tumor types, most of which (95%) are double mutation[illegible] Double PIK[illegible]ons are in c[illegible]same allel[illegible]

OPPORTUNITIES FOR IMPACT IN HUMAN GENETICS WITH PACBIO

RARE DISEASE
>50% of RID samples lack an explanation even after srWGS[1]

PHARMACOGENOMIC
35% of patients on SSRI medications see no effect[2]

NEURO
40+ neurological disorders are caused by tandem repeats[3,4]

CANCER
Complex structural variations increase risk for HBOC[5]

REPRODUCTIVE
NGS is blind to 10% of carrier screening genes[6]

TRANSPLANTS
Ultra-high-resolution HLA typing could increase 5-year survival rate by 25%[7]

1. https://www.annualreviews.org/doi/full/10.1146/annurev-genom-083118-015345
2. https://www.mdpi.com/2073-4425/11/11/1333/htm
3. https://www.nature.com/articles/nrg.2017.115
4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6485936/
5. https://jmg.bmj.com/content/early/2020/12/14/jmedgenet-2020-107320
6. https://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.1008409
7. https://www.sciencedirect.com/science/article/pii/S1083879118317014?via%3Dihub

IT'S BEEN A BUSY YEAR

INVITAE

Collaboration to accelerate long-read WGS into routine clinical care

labcorp

LabCorp scaling its HiFiViral for SARS-CoV-2 workflow; Sequel II systems deployed for global viral surveillance initiatives focused on COVID-19

PACBIO

10.1 sequencing release: 3x lower DNA input, automation. Customers seeing ~25% more HiFi data

T2T

T2T publication
HiFi sequencing enables the first complete sequence of a human genome

OMNIOME

Pacific Biosciences closes on Omniome acquisition

$900M SoftBank investment to accelerate commercial + R&D

SoftBank

Sequel IIe systems to scale up whole genome research initiatives focused on rare disease diagnosis

Children's Mercy KANSAS CITY

HiFi sequencing will be used on a cohort of rare disease cases

Rady Children's Hospital San Diego

Acquired Circulomics to extend our capabilities in extraction + sample prep

circulomics

ADDITION OF OMNIOME CAN HELP TRANSFORM GENOMICS

As only company with both LR + SR technologies we will uniquely be able to support customers with the right combination of sequencing technologies to address their needs

SBB accuracy = lower limit of detection; enables high depth/coverage applications

Better position partnership opportunities — our goal is to be best partner in the industry, and having both short and long read sequencing will help us do that

Leverage company synergies to accelerate product development + improve commercialization

ADVANCEMENTS IN PACBIO WORKFLOWS OPEN NEW APPLICATIONS

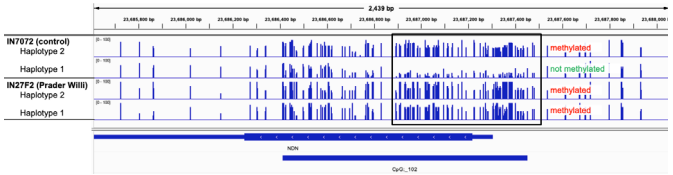
COMING SOON

Scalable whole genome sequencing

- Faster, simpler sample prep; reduce 8 hrs today to 3 hrs
- Bead-based size selection
- Reduced DNA input levels
- Kitted workflow launch expected 4Q21

Simultaneous epigenetic detection

- Analysis tools currently available to research collaborators
- Product launch expected in 1H22



PACBIO AT ASHG

PACBIO FIRESIDE CHAT
Tuesday, October 19, 12:30 pm EDT

With long reads *and* short reads, the possibilities are endless.

With the September closing of PacBio's acquisition of Omniome, PacBio intends to become the first company to offer both long-read and short-read sequencing platforms. Join us live for a 30-minute intimate conversation with genomics leaders, Christian Henry and Richard Shen, as they share their vision for the future as a combined company.

Christian Henry
President and CEO, PacBio

Richard Shen
President, Omniome

POSTER PRESENTATIONS

3534	Towards isoform resolution single-cell transcriptomics for clinical applications using highly accurate long-read sequencing	E. Tseng
3540	Long-read amplicon sequencing of the polymorphic CYP2D6 locus	L. Zhu
3623	Simplified and robust library construction for high-throughput HiFi sequencing for human varient detection	H. Dhillon
3801	Resolving complex pathogenic allleles using HiFi sequencing for long-range amplicon data with a new clustering algorithm	J. Harting
3845	Targeting clinically significant dark regions of the human genome with high-accuracy, long-read sequencing	I. McLaughlin
3860	Development and optimization of a 43-gene pharmacogenomic panel using enrichment-based capture and PacBio Hifi sequencing	D. Portik

PLATFORM PRESENTATIONS

1062	A high-resolution panel for uncovering repeat expansions that cause ataxias	Y. Tsai

COLAB THEATER TALKS
Wednesday, 10/20 9:30 am PT

Allele-specific RNA-Seq analysis on concatenated single-cell molecules

Elizabeth Tseng, Ph.D.
Associate Director, Product Marketing, PacBio

Using Long-read sequencing for haplotyping and phasing of PGX alleles

Nina Gonzaludo, Ph.D.
Sr. Manager, PGx + HLA Market Development, PacBio

LIGHTNING TALKS
Wednesday, 10/20 12:15 pm PT

Methylation detection with PacBio HiFi sequencing

Aaron Wenger, Ph.D.
Associate Director, Product Marketing, PacBio

HiFiViral: A novel method for surveillance of SARS-CoV-2 that is robust across sample input quantities and the evolution of new variants

Sarah B Kingan, Ph.D
Senior Staff Product Manager, PacBio

INTRODUCING OUR WORKSHOP SPEAKERS

INTEGRATED RARE DISEASE GENOMICS USING LONG-READ GENOME SEQUENCING

Emily G. Farrow, Ph.D., CGC
Director, Laboratory Operations,
Genomic Medicine Center, Children's Mercy Kansas City

SCALABLE RNA ISOFORM SEQUENCING USING INTRAMOLECULAR MULTIPLEXED CDNAS

Aziz Al'Khafaji, Ph.D.
Postdoctoral Associate,
Broad Institute

UNCOVERING NEUROLOGICAL DISORDERS THROUGH AN EXAMINATION OF VNTRS

Henne Holstege, Ph.D.
Assistant Professor, Amsterdam University Medical Center

ENABLING THE PROMISE OF GENOMICS TO BETTER HUMAN HEALTH

We create the world's most advanced sequencing technologies.

PACBIO®

www.pacb.com