



The Overview of Publications Based on DNBSEQ Platform





About MGI

MGI Tech Co., Ltd. (referred to as MGI) is committed to building core tools and technology to lead life science through intelligent innovation. MGI focuses on R&D, production and sales of DNA sequencing instruments, reagents, and related products to support life science research, agriculture, precision medicine and healthcare. MGI is a leading producer of clinical high-throughput gene sequencers, and its multi-omics platforms include genetic sequencing, mass spectrometry, medical imaging, and laboratory automation.

Founded in 2016, MGI has more than 1000 employees, nearly half of whom are R&D personnel. MGI operates in 26 countries and regions and has established multiple research and production bases around the world. Providing real-time, comprehensive, life-long solutions, its vision is to enable effective and affordable healthcare solutions for all.



DNBSEQ™ Sequencing Platform



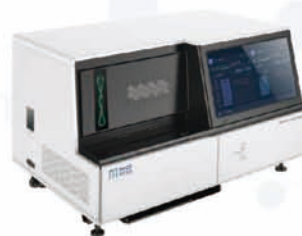
DNBSEQ-T7
Genetic Sequencer



MGISEQ-200
Genetic Sequencer



MGISEQ-2000
Genetic Sequencer



MGISEQ-2000 FAST
Genetic Sequencer

Product Model	DNBSEQ-T7	DNBSEQ-G400	DNBSEQ-G50	DNBSEQ-G400 FAST
Features	Ultra-high Throughput	Adaptive	Effective	Fast
Applications	Whole Genome Sequencing, Deep Exome Sequencing, Transcriptome Sequencing, and Targeted Panel Projects.	WGS, WES, Transcriptome sequencing and more.	Targeted DNA, RNA, Microbial sequencing.	Targeted DNA, RNA, Epigenetics and clinical applications
Flow Cell Type	FC	FCL & FCS	FCS	FCS
Lane/Flow Cell++	1 lane	2 & 4 lane	1 lane	2 lane
Operation Mode	Ultra-high Throughput	High Throughput	Medium Throughput	Medium Throughput
Max. Throughput / RUN	6Tb	1440Gb	60Gb	330Gb
Effective Reads / Flow Cell	5000M	1500-1800M	300M	550M
Average run time	PE150 within 24 hours	~38 hours	12-48 hours	12-37 hours
Min. Read Length	PE100	SE50	SE50	SE100
Max. Read Length	PE150	SE400	SE100	PE150

INTRODUCTION TO DNBSEQ™ SEQUENCING TECHNOLOGY

MGI's DNA sequencing instruments utilize the state of art core technology called DNBSEQ™. DNBSEQ™ includes all technology related to DNA nanoballs (DNB), such as DNA single strand circularization and DNB preparation technology, Patterned Arrays, DNB loading, cPAS (combinatorial Probe Anchor Synthesis), Pair-End Sequencing technology on DNB's, fluidics and detection systems, base calling algorithms, etc. CoolMPS is an advanced technology developed from cPAS. cPAS technology has been widely used on various sequencing platforms including DNBSEQ-G50, DNBSEQ-G400, DNBSEQ-T7, etc. In addition, MGI has developed a series of automated sample preparation systems and libraries preparation kits for total solutions of various applications.

DNB

DNB is the unique technology that allows DNA linear amplification in a single-tube solution. The workflow includes DNA fragmentation, adapter ligation and single-stranded circulation to produce DNB.

► High intensity of fluorescent signals and high sequencing accuracy

RCR increases the quantity of "DNA fragments (to be processed)" and thus enhance the intensity of fluorescent signals and accuracy.

► Zero-error accumulation using RCR

RCR enables each copy to be amplified from the original template and generate no accumulated replication errors, delivering high sequencing accuracy.

► Maximized efficiency of DNA loading on patterned array



Patterned array

Patterned array is the key in DNB loading technology. The coating surface of the semiconductor chip makes each loading spot positively charged. Therefore, negatively charged DNB can easily attach to the positively charged chip surface through electrostatic adhesion. Patterned array ensures each spot is attached to a single DNB and thus prevents the signal interference. Overall, patterned array enables high sequencing accuracy and high chip utilization.

► Increasing sequencing signals using nanoscale patterned chip

The Patterned Array of spots on Flow Cells prevents cross interference between fluorescent signals and enable high intensity of signals.

► Precision machined semiconductor chip enhances the attachment of DNB to chip

The size of DNB matches the area of effective spot on the chip.

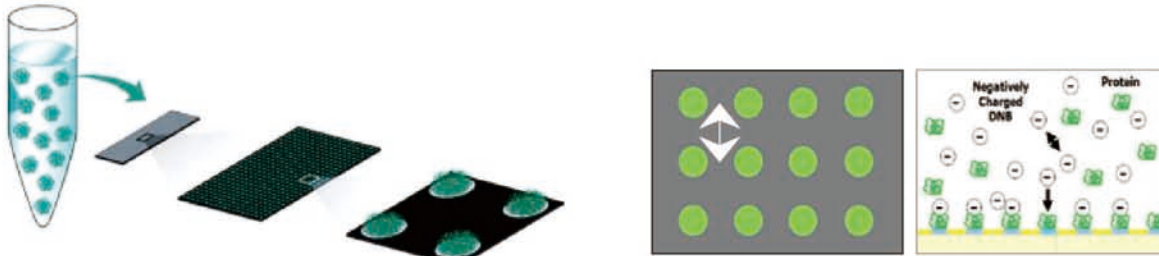
Thus, each spot is only attached to a single DNB, avoiding the signal interference.

► Precise pattern enables efficient imaging system and DNB loading

Patterned array and DNB technology maximize the utilization of imaging system and chip surface area, and sequencing accuracy.

► Low Duplication , No Index Hopping

DNB is amplified in solution and loaded without PCR reagents. Hence the duplicate rate is extremely low using DNB technology and patterned array.



cPAS

cPAS is the innovative technology developed by BGI. By improving combinatorial Probe-Ancor Ligation(cPAL), cPAS increases the sequencing accuracy with higher speed and read length of sequencing.

► MGI proprietary enzymes react completely with 60 seconds

Our biochemistry team has studied a large quantity of reaction conditions and screened tens of thousands of sequencing enzymes to successfully complete biochemical reactions within just 60 seconds.

► Real-time sub-pixel registration, image processing and base calling

Advanced Real-time Image Processing software, Sub-pixel Registration and Multi-thread Parallel Compression Algorithms result in accurate real-time imaging and base calling and high industry-leading data-processing speed. Furthermore, GPU empowers DNBSEQ-G400 with high speed to analyze high empowers DNBSEQ-G400 with high speed to analyze high

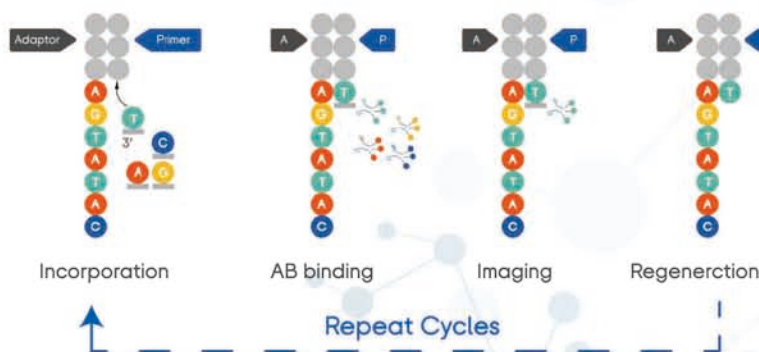
► CoolMPS

CoolMPS Fluorescent labeling of dNTPs and capture of nucleotide signal are key steps in high-throughput sequencing. CoolMPS sequencing chemistry is a novel antibody-based sequencing product. The dNTPs of CoolMPS are without fluorescent labeled (called "cold dNTPs") which incorporated into the sequencing strand by DNA polymerase, and base calling is achieved by specific binding of fluorescently labeled antibodies. During this process, the incorporated bases are unmodified, ultimately resulting in clearer base calling.

Cleaner

Brighter

Longer



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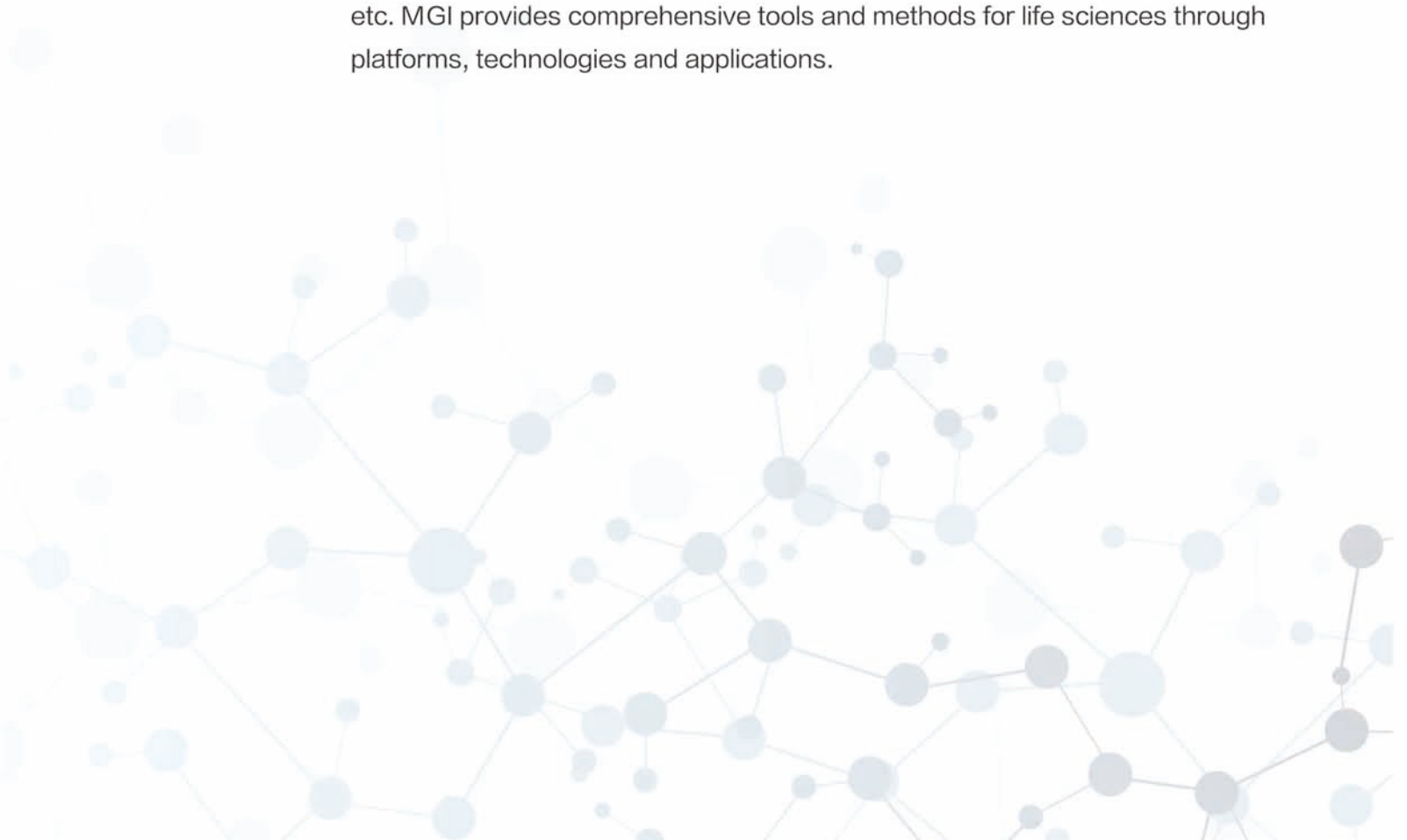


DNBSEQ Platform Technologies

———— (Comparison and Innovation)

MGI has successively released a variety of high, medium, and low throughput gene sequencing instruments, which support lots of sequencing methods such as whole-exome, whole-genome, transcriptome, Single-cell transcriptome, Metagenome, and Small RNA sequencing etc. Many studies indicate that the data produced by BGI's sequencing instruments in various sequencing methods are comparable to those from the similar sequencing instruments on the market.

In addition, based on the DNBSEQ sequencing platform, MGI also has breakthroughs on technological innovations, including single-tube Long Fragment Read (stLFR), a library construction technology with single-tube lengths up to 300Kb, single-cell Chromatin Accessibility and Transcriptome sequencing (scCAT-seq), and Controlled Polymerizations by Adapter-Ligation (CP-AL) etc. MGI provides comprehensive tools and methods for life sciences through platforms, technologies and applications.



Systematic comparison of germline variant calling pipelines cross multiple next-generation sequencers

Publications: Scientific Reports, 2019

Author Affiliation

South China University of Technology

Abstract

The development and innovation of next generation sequencing (NGS) and the subsequent analysis tools have gain popularity in scientific researches and clinical diagnostic applications. Hence, a systematic comparison of the sequencing platforms and variant calling pipelines could provide significant guidance to NGS-based scientific and clinical genomics. In this study, we compared the performance, concordance and operating efficiency of 27 combinations of sequencing platforms and variant calling pipelines, testing three variant calling pipelines-Genome Analysis Tool Kit Haplotype Caller, Strelka2 and Samtools-Var-scan2 for nine data sets for the NA12878 genome sequenced by different platforms including BGISEQ500, MGISEQ2000, HiSeq4000, NovaSeq and HiSeq Xten. For the variants calling performance of 12 combinations in WES datasets, all combinations displayed good performance in calling SNPs, with their F-scores entirely higher than 0.96, and their performance in calling INDELs varies from 0.75 to 0.91. And all 15 combinations in WGS datasets also manifested good performance, with F-scores in calling SNPs were entirely higher than 0.975 and their performance in calling INDELs varies from 0.71 to 0.93. All of these combinations manifested high concordance in variant identification, while the divergence of variants identification in WGS datasets were larger than that in WES datasets. We also down-sampled the original WES and WGS datasets at a series of gradient coverage across multiple platforms, then the variants calling period consumed by the three pipelines at each coverage were counted, respectively. For the GIAB datasets on both BGI and Illumina platforms, Strelka2 manifested its ultra-performance in detecting accuracy and processing efficiency compared with other two pipelines on each sequencing platform, which was recommended in the further promotion and application of next generation sequencing technology. The results of our researches will provide useful and comprehensive guidelines for personal or organizational researchers in reliable and consistent variants identification.

Reference

Chen J, Li X, Zhong H, et al. Systematic comparison of germline variant calling pipelines cross multiple next-generation sequencers[J]. Scientific Reports, 2019, 9(1): 9345.

A new massively parallel nanoball sequencing platform for whole exome research

Publications: BMC Bioinformatics, 2019

Author Affiliation

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Abstract

BACKGROUND:

Whole exome sequencing (WES) has been widely used in human genetics research. BGISEQ-500 is a recently established next-generation sequencing platform. However, the performance of BGISEQ-500 on WES is not well studied. In this study, we evaluated the performance of BGISEQ-500 on WES by side-to-side comparison with Hiseq4000, on well-characterized human sample NA12878.

RESULTS:

BGISEQ demonstrated similarly high reproducibility as Hiseq for variation detection. Also, the SNVs from BGISEQ data is highly consistent with Hiseq results (concordance 96.5%~ 97%). Variation detection accuracy was subsequently evaluated with data from the genome in a bottle project as the benchmark. Both platforms showed similar sensitivity and precision in SNV detection. While in indel detection, BGISEQ showed slightly higher sensitivity and lower precision. The impact of sequence depth and read length on variation detection accuracy was further analyzed, and showed that variation detection sensitivity still increasing when the sequence depth is larger than 100x, and the impact of read length is minor when using 100x data.

CONCLUSIONS:

This study suggested that BGISEQ-500 is a qualified sequencing platform for WES.

Reference

Xu Y, Lin Z, Tang C, et al. A new massively parallel nanoball sequencing platform for whole exome research[J]. BMC bioinformatics, 2019, 20(1): 153.

Impact of sequencing depth and technology on de novo RNA-Seq assembly

Publications: BMC Genomics, 2019

Author Affiliation

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Abstract

BACKGROUND:

RNA-Seq data is inherently nonuniform for different transcripts because of differences in gene expression. This makes it challenging to decide how much data should be generated from each sample. How much should one spend to recover the less expressed transcripts? The sequencing technology used is another consideration, as there are inevitably always biases against certain sequences. To investigate these effects, we first looked at high-depth libraries from a set of well-annotated organisms to ascertain the impact of sequencing depth on de novo assembly. We then looked at libraries sequenced from the Universal Human Reference RNA (UHRR) to compare the performance of Illumina HiSeq and MGI DNBseq™ technologies.

RESULTS:

On the issue of sequencing depth, the amount of exomic sequence assembled plateaued using data sets of approximately 2 to 8 Gbp. However, the amount of genomic sequence assembled did not plateau for many of the analyzed organisms. Most of the unannotated genomic sequences are single-exon transcripts whose biological significance will be questionable for some users. On the issue of sequencing technology, both of the analyzed platforms recovered a similar number of full-length transcripts. The missing "gap" regions in the HiSeq assemblies were often attributed to higher GC contents, but this may be an artefact of library preparation and not of sequencing technology.

CONCLUSIONS:

Increasing sequencing depth beyond modest data sets of less than 10 Gbp recovers a plethora of single-exon transcripts undocumented in genome annotations. DNBseq™ is a viable alternative to HiSeq for de novo RNA-Seq assembly.

Reference

Patterson J, Carpenter E J, Zhu Z, et al. Impact of sequencing depth and technology on de novo RNA-Seq assembly[J]. BMC genomics, 2019, 20(1): 604.

cPAS-based sequencing on the BGISEQ-500 to explore small non-coding RNAs

Publications: Clinical Epigenetics, 2016

Author Affiliation

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Abstract

BACKGROUND:

We present the first sequencing data using the combinatorial probe-anchor synthesis (cPAS)-based BGISEQ-500 sequencer. Applying cPAS, we investigated the repertoire of human small non-coding RNAs and compared it to other techniques.

RESULTS:

Starting with repeated measurements of different specimens including solid tissues (brain and heart) and blood, we generated a median of 30.1 million reads per sample. 24.1 million mapped to the human genome and 23.3 million to the miRBase. Among six technical replicates of brain samples, we observed a median correlation of 0.98. Comparing BGISEQ-500 to HiSeq, we calculated a correlation of 0.75. The comparability to microarrays was similar for both BGISEQ-500 and HiSeq with the first one showing a correlation of 0.58 and the latter one correlation of 0.6. As for a potential bias in the detected expression distribution in blood cells, 98.6% of HiSeq reads versus 93.1% of BGISEQ-500 reads match to the 10 miRNAs with highest read count. After using miRDeep2 and employing stringent selection criteria for predicting new miRNAs, we detected 74 high-likely candidates in the cPAS sequencing reads prevalent in solid tissues and 36 candidates prevalent in blood.

CONCLUSIONS:

While there is apparently no ideal platform for all challenges of miRNome analyses, cPAS shows high technical reproducibility and supplements the hitherto available platforms.

Reference

Fehlmann T, Reinheimer S, Geng C, et al. cPAS-based sequencing on the BGISEQ-500 to explore small non-coding RNAs[J]. Clinical epigenetics, 2016, 8(1): 123.

Comparative analysis of sequencing technologies platforms for single-cell transcriptomics

Publications: GENOME BIOLOGY, 2018

Author Affiliation

Wellcome Genome Campus | University of Southern Denmark | BGI-Shenzhen |
Southeast University | South China University of Technology | Cambridge University

Abstract

Single-cell RNA-seq technologies require library preparation prior to sequencing. Here, we present the first report to compare the cheaper BGISEQ-500 platform to the Illumina HiSeq platform for scRNA-seq. We generate a resource of 468 single cells and 1297 matched single cDNA samples, performing SMARTer and Smart-seq2 protocols on two cell lines with RNA spike-ins. We sequence these libraries on both platforms using single- and paired-end reads. The platforms have comparable sensitivity and accuracy in terms of quantification of gene expression, and low technical variability. Our study provides a standardized scRNA-seq resource to benchmark new scRNA-seq library preparation protocols and sequencing platforms.

Reference

Natarajan K N, Miao Z, Jiang M, et al. Comparative analysis of sequencing technologies platforms for single-cell transcriptomics[J]. bioRxiv, 2018: 463117.

Assessment of the cPAS-based BGISEQ-500 platform for metagenomic sequencing

Publications: Giga Science, 2017

Author Affiliation

BGI-Shenzhen | China National GeneBank | University of Copenhagen | Harvard Medical School | Harvard University | Joslin Diabetes Center | Dana-Farber Cancer Institute | Harvard TH Chan School of Public Health | James D. Watson Institute of Genome Sciences, Zhejiang | Clinical University Hospital, Huddinge | South China University of Technology

Abstract

BACKGROUND:

More extensive use of metagenomic shotgun sequencing in microbiome research relies on the development of high-throughput, cost-effective sequencing. Here we present a comprehensive evaluation of the performance of the new high-throughput sequencing platform BGISEQ-500 for metagenomic shotgun sequencing and compare its performance with that of 2 Illumina platforms.

FINDINGS:

Using fecal samples from 20 healthy individuals, we evaluated the intra-platform reproducibility for metagenomic sequencing on the BGISEQ-500 platform in a setup comprising 8 library replicates and 8 sequencing replicates. Cross-platform consistency was evaluated by comparing 20 pairwise replicates on the BGISEQ-500 platform vs the Illumina HiSeq 2000 platform and the Illumina HiSeq 4000 platform. In addition, we compared the performance of the 2 Illumina platforms against each other. By a newly developed overall accuracy quality control method, an average of 82.45 million high-quality reads (96.06% of raw reads) per sample, with 90.56% of bases scoring Q30 and above, was obtained using the BGISEQ-500 platform. Quantitative analyses revealed extremely high reproducibility between BGISEQ-500 intra-platform replicates. Cross-platform replicates differed slightly more than intra-platform replicates, yet a high consistency was observed. Only a low percentage (2.02%–3.25%) of genes exhibited significant differences in relative abundance comparing the BGISEQ-500 and HiSeq platforms, with a bias toward genes with higher GC content being enriched on the HiSeq platforms.

CONCLUSIONS:

Our study provides the first set of performance metrics for human gut metagenomic sequencing data using BGISEQ-500. The high accuracy and technical reproducibility confirm the applicability of the new platform for metagenomic studies, though caution is still warranted when combining metagenomic data from different platforms.

Reference

Fang C, Zhong H, Lin Y, et al. Assessment of the cPAS-based BGISEQ-500 platform for metagenomic sequencing[J]. Gigascience, 2017, 7(3): gix133.

Efficient and unique co-barcoding of second-generation sequencing reads from long DNA molecules enabling cost effective and accurate sequencing, haplotyping, and de novo assembly

Publications: GENOME RESEARCH, 2019

Author Affiliation

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Advanced Genomics Technology Laboratory, Complete Genomics Incorporated |

James D. Watson Institute of Genome Sciences

Abstract

Here, we describe single-tube long fragment read (stLFR), a technology that enables sequencing of data from long DNA molecules using economical second-generation sequencing technology. It is based on adding the same barcode sequence to subfragments of the original long DNA molecule (DNA cobarcoding). To achieve this efficiently, stLFR uses the surface of microbeads to create millions of miniaturized barcoding reactions in a single tube. Using a combinatorial process, up to 3.6 billion unique barcode sequences were generated on beads, enabling practically nonredundant cobarcoding with 50 million barcodes per sample. Using stLFR, we demonstrate efficient unique cobarcoding of more than 8 million 20- to 300-kb genomic DNA fragments. Analysis of the human genome NA12878 with stLFR demonstrated high-quality variant calling and phase block lengths up to N50 34 Mb. We also demonstrate detection of complex structural variants and complete diploid de novo assembly of NA12878. These analyses were all performed using single stLFR libraries, and their construction did not significantly add to the time or cost of whole-genome sequencing (WGS) library preparation. stLFR represents an easily automatable solution that enables high-quality sequencing, phasing, SV detection, scaffolding, cost-effective diploid de novo genome assembly, and other long DNA sequencing applications.

Reference

Wang O, Chin R, Cheng X, et al. Efficient and unique cobarcoding of second-generation sequencing reads from long DNA molecules enabling cost-effective and accurate sequencing, haplotyping, and de novo assembly[J]. Genome research, 2019, 29(5): 798-808.

Deconvolution of single-cell multi-omics layers reveals regulatory heterogeneity

Publications: Nature Communications, 2019

Author Affiliation

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| National Engineering and Research Center of Human Stem Cell | University of Copenhagen | Berlin Institute of Health and Charité

Abstract

Integrative analysis of multi-omics layers at single cell level is critical for accurate dissection of cell-to-cell variation within certain cell populations. Here we report scCAT-seq, a technique for simultaneously assaying chromatin accessibility and the transcriptome within the same single cell. We show that the combined single cell signatures enable accurate construction of regulatory relationships between cis-regulatory elements and the target genes at single-cell resolution, providing a new dimension of features that helps direct discovery of regulatory patterns specific to distinct cell identities. Moreover, we generate the first single cell integrated map of chromatin accessibility and transcriptome in early embryos and demonstrate the robustness of scCAT-seq in the precise dissection of master transcription factors in cells of distinct states. The ability to obtain these two layers of omics data will help provide more accurate definitions of "single cell state" and enable the deconvolution of regulatory heterogeneity from complex cell populations.

Reference

Liu L, Liu C, Quintero A, et al. Deconvolution of single-cell multi-omics layers reveals regulatory heterogeneity[J]. Nature communications, 2019

Development of coupling controlled polymerizations by adapter-ligation in mate-pair sequencing for detection of various genomic variants in one single assay

Publications: DNA RESEARCH, 2019

Author Affiliation

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Guangdong High-Throughput Sequencing Research Center |
James D. Watson Institute of Genome Sciences, Zhejiang |
The Chinese University of Hong Kong-Baylor College of Medicine Joint Center for Medical Genetics

Abstract

The diversity of disease presentations warrants one single assay for detection and delineation of various genomic disorders. Herein, we describe a gel-free and biotin-capture-free mate-pair method through coupling Controlled Polymerizations by Adapter-Ligation (CP-AL). We first demonstrated the feasibility and ease-of-use in monitoring DNA nick translation and primer extension by limiting the nucleotide input. By coupling these two controlled polymerizations by a reported non-conventional adapter-ligation reaction 3' branch ligation, we evidenced that CP-AL significantly increased DNA circularization efficiency (by 4-fold) and was applicable for different sequencing methods but at a fraction of current cost. Its advantages were further demonstrated by fully elimination of small-insert-contaminated (by 39.3-fold) with a 50% increment of physical coverage, and producing uniform genome/exome coverage and the lowest chimeric rate. It achieved single-nucleotide variants detection with sensitivity and specificity up to 97.3 and 99.7%, respectively, compared with data from small-insert libraries. In addition, this method can provide a comprehensive delineation of structural rearrangements, evidenced by a potential diagnosis in a patient with oligo-atheno-terato-spermia. Moreover, it enables accurate mutation identification by integration of genomic variants from different aberration types. Overall, it provides a potential single-integrated solution for detecting various genomic variants, facilitating a genetic diagnosis in human diseases.

Reference

Dong Z, Zhao X, Li Q, Yang Z, Xi Y, Alexeev A, et al. Development of coupling controlled polymerizations by adapter-ligation in mate-pair sequencing for detection of various genomic variants in one single assay. *DNA Res.* 2019. Epub 2019/06/08. doi: 10.1093/dnares/dsz011. PubMed PMID: 31173071.



DNBSEQ Platform Application

MGI's DNBSEQ sequencing platform has been expanding its application field on research and products. At present, the published papers based on the MGI DNBSEQ sequencing platform involve over 200 species and samples, covering animals, plants, microorganisms, and disease research etc.

(1) In disease research, MGI conducts comprehensive research from the level of DNA, RNA, epigenetics, and metagenomics, and simultaneously combines with various information related to phenotype (environment, age, disease treatment history, family history, susceptibility, etc.), which lays an important foundation for fully revealing the human genetics mechanism.

(2) In animal and plant research, single-tube Long Fragment Read (stLFR), the unique technology on DNBSEQ sequencing platform, is applied to study the whole-genome of *Spodoptera frugiperda* invading China, which promotes the scientific control of *Spodoptera frugiperda*, improves the control efficiency, and reduces its potential harm.

(3) In microbial research, scientists carry out sequencing analysis and research on microorganisms such as pathogens and intestinal flora through the DNBSEQTM platform, promoting the research progress of infectious disease prevention and control.

Dissecting primate early post-implantation development using long-term in vitro embryo culture

Publications: Science, 2019

Author Affiliation

Kunming University of Science and Technology | BGI-Shenzhen | China National GeneBank | University of Texas Southwestern Medical Center | Salk Institute for Biological Studies | Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences (CAS), University of Chinese Academy of Sciences, Shanghai | CAS Key Laboratory of Regenerative Biology, Guangdong Provincial Key Laboratory of Stem Cell and Regenerative Medicine, Guangzhou | Guangzhou Institutes of Biomedicine and Health Guangzhou Regenerative Medicine and Health Guangdong Laboratory (GRMH-GDL) | CAS Center for Excellence in Brain Science and Intelligence Technology, CAS, Shanghai

Abstract

The transition from peri-implantation to gastrulation in mammals entails the specification and organization of the lineage progenitors into a body plan. Technical and ethical challenges have limited understanding of the cellular and molecular mechanisms that underlie this transition. We established a culture system that enabled the development of cynomolgus monkey embryos in vitro for up to 20 days. Cultured embryos underwent key primate developmental stages, including lineage segregation, bilaminar disc formation, amniotic and yolk sac cavitation, and primordial germ cell-like cell (PGCLC) differentiation. Single-cell RNA-sequencing analysis revealed development trajectories of primitive endoderm, trophoctoderm, epiblast lineages, and PGCLCs. Analysis of single-cell chromatin accessibility identified transcription factors specifying each cell type. Our results reveal critical developmental events and complex molecular mechanisms underlying nonhuman primate embryogenesis in the early postimplantation period, with possible relevance to human development.

Reference

Niu Y, Sun N, Li C, et al. Dissecting primate early post-implantation development using long-term in vitro embryo culture[J]. Science, 2019.

Prenatal Diagnosis of Fetuses with Increased Nuchal Translucency by Genome Sequencing Analysis

Publications: Frontiers in Genetics, 2019

Author Affiliation

Department of Obstetrics & Gynaecology, The Chinese University of Hong Kong | The Chinese University of Hong Kong-Baylor College of Medicine Joint Center for Medical Genetics | Bao'an Maternity and Child Healthcare Hospital Affiliated to Jinan University School of Medicine | The Third Affiliated Hospital of Guangzhou Medical University | Baylor College of Medicine

Abstract

Background: Increased nuchal translucency (NT) is an important biomarker associated with increased risk of fetal structural anomalies. It is known to be contributed by a wide range of genetic etiologies from single-nucleotide variants to those affecting millions of base pairs. Currently, prenatal diagnosis is routinely performed by karyotyping and chromosomal microarray analysis (CMA); however, both of them have limited resolution. The diversity of the genetic etiologies warrants an integrated assay such as genome sequencing (GS) for comprehensive detection of genomic variants. Herein, we aim to evaluate the feasibility of applying GS in prenatal diagnosis for the fetuses with increased NT.

Methods: We retrospectively applied GS (> 30-fold) for fetuses with increased NT (≥ 3.5 mm) who underwent routine prenatal diagnosis. Detection of single-nucleotide variants, copy number variants, and structural rearrangements was performed simultaneously, and the results were integrated for interpretation in accordance with the guidelines of the American College of Medical Genetics and Genomics. Pathogenic or likely pathogenic (P/LP) variants were selected for validation and parental confirmation, when available.

Results: Overall, 50 fetuses were enrolled, including 34 cases with isolated increased NT and 16 cases with other fetal structural malformations. Routine CMA and karyotyping reported eight P/LP CNVs, yielding a diagnostic rate of 16.0% (8/50). In comparison, GS provided a twofold increase in diagnostic yield (32.0%, 16/50), including one mosaic turner syndrome, eight cases with microdeletions/microduplications, and seven cases with P/LP point mutations. Moreover, GS identified two cryptic insertions and two inversions. Follow-up study further demonstrated the potential pathogenicity of an apparently balanced insertion that disrupted an OMIM autosomal dominant disease-causing gene at the insertion site.

Conclusions: Our study demonstrates that applying GS in fetuses with increased NT can comprehensively detect and delineate the various genomic variants that are causative to the diseases. Importantly, prenatal diagnosis by GS doubled the diagnostic yield compared with routine protocols. Given a comparable turnaround time and less DNA required, our study provides strong evidence to facilitate GS in prenatal diagnosis, particularly in fetuses with increased NT.

Reference

Choy K W, Wang H, Shi M, et al. Prenatal Diagnosis of Fetuses with Increased Nuchal Translucency by Genome Sequencing Analysis[J]. Frontiers in genetics, 2019, 10: 761.

Development and Validation of Tumor-educated Blood Platelets Integrin Alpha 2b (ITGA2B) RNA for Diagnosis and Prognosis of Non-small-cell Lung Cancer through RNA-seq

Publications: International Journal of Biological Sciences, 2019

Author Affiliation

Sun Yat-sen University Cancer Center | The Sixth Affiliated Hospital, Sun Yat-sen University |
Affiliated Tumor Hospital of Zhengzhou University

Abstract

Background: Currently, there are no molecular biomarkers for the early detection of non-small-cell lung cancer (NSCLC). This study focused on identifying RNAs found on tumor-educated blood platelets (TEPs) for detecting stage I NSCLC.

Methods: Platelet RNAs, isolated from the blood of 9 patients with NSCLC (stages I and II) and 8 healthy controls, were analyzed using RNA-seq. ITGA2B was selected as a candidate marker. Two different Polymerase Chain Reactions (PCR) were used to measure ITGA2B in platelet samples from healthy controls (n = 150), patients with NSCLC (n = 243), and patients with benign pulmonary nodules (n = 141) in two cohorts.

Results: Platelet ITGA2B levels were significantly higher ($p < 0.001$) in patients with NSCLC than in all controls. The diagnostic accuracy of ITGA2B was area under the curve (AUC) of 0.922 [95% confidence interval (CI), 0.892–0.952], sensitivity of 92.8%, and specificity of 78.6% in the test cohort and 0.888, 91.2%, and 56.5% in the validation cohort for NSCLC by quantitative real time PCR (q-PCR). Furthermore, ITGA2B maintained diagnostic accuracy for patients with NSCLC using Droplet Digital PCR (ddPCR) and the other type of internal control, Ribosomal Protein L32 (RPL32) [ddPCR: 0.967 (0.929–1.000) and RPL32: 0.847(0.773–0.920)]. A nomogram incorporating ITGA2B, carcinoembryonic antigen (CEA) and stage could predict the overall survival (C-index = 0.756).

Conclusions: TEP ITGA2B is a promising marker to improve identification of patients with stage I NSCLC and differentiate malignant from benign lung nodules.

Reference

Xing S, Zeng T, Xue N, et al. Development and Validation of Tumor-educated Blood Platelets Integrin Alpha 2b (ITGA2B) RNA for Diagnosis and Prognosis of Non-small-cell Lung Cancer through RNA-seq[J]. International journal of biological sciences, 2019, 15(9): 1977.

ABCA4 Gene Screening in a Chinese Cohort With Stargardt Disease: Identification of 37 Novel Variants

Publications: *Frontiers in Genetics*, 2019

Author Affiliation

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Abstract

Purpose: To clarify the mutation spectrum and frequency of ABCA4 in a Chinese cohort with Stargardt disease (STGD1).

Methods: A total of 153 subjects, comprising 25 families (25 probands and their family members) and 71 sporadic cases, were recruited for the analysis of ABCA4 variants. All probands with STGD1 underwent a comprehensive ophthalmologic examination. Overall, 792 genes involved in common inherited eye diseases were screened for variants by panel-based next-generation sequencing (NGS). Variants were filtered and analyzed to evaluate possible pathogenicity.

Results: The total variant detection rate of at least one ABCA4 mutant allele was 84.3% (129/153): two or three disease-associated variants in 86 subjects (56.2%), one mutant allele in 43 subjects (28.1%), and no variants in 24 subjects (15.7%). Ninety-six variants were identified in the total cohort, which included 62 missense (64%), 15 splicing (16%), 11 frameshift (12%), 6 nonsense (6%), and 2 small insertion or deletion (2%) variants. Thirty-seven novel variants were found, including a de novo variant, c.4561delA. The most prevalent variant was c.101_106delCTTTAT (10.5%), followed by c.2894A > G (6.5%) and c.6563T > C (4.6%), in STGD1 patients from eastern China.

Conclusion: Thirty-seven novel variants were detected using panel-based NGS, including one de novo variant, further extending the mutation spectrum of ABCA4. The common variants in a population from eastern China with STGD1 were also identified.

Reference

Hu F, Li J, Gao F, et al. ABCA4 gene screening in a Chinese cohort with Stargardt disease: Identification of 37 novel variants[J]. *Frontiers in genetics*, 2019, 10: 773.

C/EBP β enhances platinum resistance of ovarian cancer cells by reprogramming H3K79 methylation

Publications: Nature Communications, 2018

Author Affiliation

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Abstract

Chemoresistance is a major unmet clinical obstacle in ovarian cancer treatment. Epigenetics plays a pivotal role in regulating the malignant phenotype, and has the potential in developing therapeutically valuable targets that improve the dismal outcome of this disease. Here we show that a series of transcription factors, including C/EBP β , GCM1, and GATA1, could act as potential modulators of histone methylation in tumor cells. Of note, C/EBP β , an independent prognostic factor for patients with ovarian cancer, mediates an important mechanism through which epigenetic enzyme modifies groups of functionally related genes in a context-dependent manner. By recruiting the methyltransferase DOT1L, C/EBP β can maintain an open chromatin state by H3K79 methylation of multiple drug-resistance genes, thereby augmenting the chemoresistance of tumor cells. Therefore, we propose a new path against cancer epigenetics in which identifying and targeting the key regulators of epigenetics such as C/EBP β may provide more precise therapeutic options in ovarian cancer.

Reference

Liu D, Zhang X X, Li M C, et al. C/EBP β enhances platinum resistance of ovarian cancer cells by reprogramming H3K79 methylation[J]. Nature communications, 2018, 9(1): 1739.

Subgenomic flavivirus RNA binds the mosquito DEAD/H-box helicase ME31B and determines Zika virus transmission by *Aedes aegypti*

Publications: PNAS, 2019

Author Affiliation

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Abstract

Zika virus (ZIKV) is an arthropod-borne flavivirus predominantly transmitted by *Aedes aegypti* mosquitoes and poses a global human health threat. All flaviviruses, including those that exclusively replicate in mosquitoes, produce a highly abundant, noncoding subgenomic flavivirus RNA (sfRNA) in infected cells, which implies an important function of sfRNA during mosquito infection. Currently, the role of sfRNA in flavivirus transmission by mosquitoes is not well understood. Here, we demonstrate that an sfRNA-deficient ZIKV (ZIKV Δ SF1) replicates similar to wild-type ZIKV in mosquito cell culture but is severely attenuated in transmission by *Ae. aegypti* after an infectious blood meal, with 5% saliva-positive mosquitoes for ZIKV Δ SF1 vs. 31% for ZIKV. Furthermore, viral titers in the mosquito saliva were lower for ZIKV Δ SF1 as compared to ZIKV. Comparison of mosquito infection via infectious blood meals and intrathoracic injections showed that sfRNA is important for ZIKV to overcome the mosquito midgut barrier and to promote virus accumulation in the saliva. Next-generation sequencing of infected mosquitoes showed that viral small-interfering RNAs were elevated upon ZIKV Δ SF1 as compared to ZIKV infection. RNA-affinity purification followed by mass spectrometry analysis uncovered that sfRNA specifically interacts with a specific set of *Ae. aegypti* proteins that are normally associated with RNA turnover and protein translation. The DEAD/H-box helicase ME31B showed the highest affinity for sfRNA and displayed antiviral activity against ZIKV in *Ae. aegypti* cells. Based on these results, we present a mechanistic model in which sfRNA sequesters ME31B to promote flavivirus replication and virion production to facilitate transmission by mosquitoes.

Reference

Göertz G P, van Bree J W M, Hiralal A, et al. Subgenomic flavivirus RNA binds the mosquito DEAD/H-box helicase ME31B and determines Zika virus transmission by *Aedes aegypti*[J]. Proceedings of the National Academy of Sciences, 2019, 116(38): 19136–19144.

Altered respiratory virome and serum cytokine profile associated with recurrent respiratory tract infections in children

Publications: Nature Communications, 2019

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Abstract

Recurrent acute respiratory tract infections (ARTIs) affect a large population, yet the specific decisive factors are largely unknown. Here we study a population of 4407 children diagnosed with ARTI, comparing respiratory virome and serum cytokine profiles associated with multiple ARTIs and single ARTI during a six-year period. The relative abundance of *Propionibacterium* phages is significantly elevated in multiple ARTIs compared to single ARTI group. Serum levels of TIMP-1 and PDGF-BB are markedly increased in multiple ARTIs compared to single-ARTI and non-ARTI controls, making these two cytokines potential predictors for multiple ARTIs. The presence of *Propionibacterium* phages is associated with higher levels of TIMP-1 and PDGF-BB. Receiver operating characteristic (ROC) curve analyses show that the combination of TIMP-1, PDGF-BB and *Propionibacterium* phages could be a strong predictor for multiple ARTIs. These findings indicate that respiratory microbe homeostasis and specific cytokines are associated with the onset of multiple ARTIs over time.

Reference

Li Y, Fu X, Ma J, et al. Altered respiratory virome and serum cytokine profile associated with recurrent respiratory tract infections in children[J]. Nature communications, 2019, 10.

An integrated chromatin accessibility and transcriptome landscape of human pre-implantation embryos

Publications: Nature Communications, 2019

Author Affiliation

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Abstract

Human pre-implantation embryonic development involves extensive changes in chromatin structure and transcriptional activity. Here, we report on LiCAT-seq, a technique that enables simultaneous profiling of chromatin accessibility and gene expression with ultra-low input of cells, and map the chromatin accessibility and transcriptome landscapes for human pre-implantation embryos.

We observed global difference in chromatin accessibility between sperm and all stages of embryos, finding that the accessible regions in sperm tend to occur in gene-poor genomic regions. Integrative analyses between the two datasets reveals strong association between the establishment of accessible chromatin and embryonic genome activation (EGA), and uncovers transcription factors and endogenous retrovirus (ERVs) specific to EGA. In particular, a large proportion of the early activated genes and ERVs are bound by DUX4 and become accessible as early as the 2- to 4-cell stages. Our results thus offer mechanistic insights into the molecular events inherent to human pre-implantation development.

Reference

Liu L, Leng L, Liu C, et al. An integrated chromatin accessibility and transcriptome landscape of human pre-implantation embryos[J]. Nature communications, 2019, 10(1): 364.

Resequencing 545 ginkgo genomes across the world reveals the evolutionary history of the living fossil

Publications: Nature Communications, 2019

Author Affiliation

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Abstract

As Charles Darwin anticipated, living fossils provide excellent opportunities to study evolutionary questions related to extinction, competition, and adaptation. Ginkgo (*Ginkgo biloba* L.) is one of the oldest living plants and a fascinating example of how people have saved a species from extinction and assisted its resurgence. By resequencing 545 genomes of ginkgo trees sampled from 51 populations across the world, we identify three refugia in China and detect multiple cycles of population expansion and reduction along with glacial admixture between relict populations in the southwestern and southern refugia. We demonstrate multiple anthropogenic introductions of ginkgo from eastern China into different continents. Further analyses reveal bioclimatic variables that have affected the geographic distribution of ginkgo and the role of natural selection in ginkgo's adaptation and resilience. These investigations provide insights into the evolutionary history of ginkgo trees and valuable genomic resources for further addressing various questions involving living fossil species.

Reference

Zhao Y P, Fan G, Yin P P, et al. Resequencing 545 ginkgo genomes across the world reveals the evolutionary history of the living fossil[J]. Nature communications, 2019, 10(1): 1-10.

Modulating plant growth–metabolism coordination for sustainable agriculture

Publications: Nature, 2018

Author Affiliation

Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Beijing | University of Chinese Academy of Sciences, Beijing | Hebei Academy of Agriculture and Forestry Sciences | University of Oxford

Abstract

Enhancing global food security by increasing the productivity of green revolution varieties of cereals risks increasing the collateral environmental damage produced by inorganic nitrogen fertilizers. Improvements in the efficiency of nitrogen use of crops are therefore essential; however, they require an in-depth understanding of the co-regulatory mechanisms that integrate growth, nitrogen assimilation and carbon fixation. Here we show that the balanced opposing activities and physical interactions of the rice GROWTH-REGULATING FACTOR 4 (GRF4) transcription factor and the growth inhibitor DELLA confer homeostatic co-regulation of growth and the metabolism of carbon and nitrogen. GRF4 promotes and integrates nitrogen assimilation, carbon fixation and growth, whereas DELLA inhibits these processes. As a consequence, the accumulation of DELLA that is characteristic of green revolution varieties confers not only yield-enhancing dwarfism, but also reduces the efficiency of nitrogen use. However, the nitrogen-use efficiency of green revolution varieties and grain yield are increased by tipping the GRF4-DELLA balance towards increased GRF4 abundance. Modulation of plant growth and metabolic co-regulation thus enables novel breeding strategies for future sustainable food security and a new green revolution.

Reference

Li S, Tian Y, Wu K, et al. Modulating plant growth–metabolism coordination for sustainable agriculture[J]. Nature, 2018, 560(7720): 595.

The first chromosome - level genome for a marine mammal as a resource to study ecology and evolution

Publications: Molecular Ecology Resources, 2019

Author Affiliation

BGI-Qingdao, BGI-Shenzhen | University of Macau | Technical University of Denmark | China National GeneBank | Guangdong Pearl River Estuary Chinese White Dolphin National Nature Reserve Administration MGI, BGI-Shenzhen | Institute of Deep-Sea Science and Engineering, Chinese Academy of Science, Sanya Health and Family Planning Integrated Supervision Enforcement Bureau of Shinan District, Qingdao City | Guangdong Ocean University | King Abdulaziz University (KAU) | University of Copenhagen | James D. Watson Institute of Genome Sciences, Zhejiang

Abstract

Marine mammals are important models for studying convergent evolution and aquatic adaption, and thus reference genomes of marine mammals can provide evolutionary insights. Here, we present the first chromosome-level marine mammal genome assembly based on the data generated by the BGISEQ-500 platform, for a stranded female sperm whale (*Physeter macrocephalus*). Using this reference genome, we performed chromosome evolution analysis of the sperm whale, including constructing ancestral chromosomes, identifying chromosome rearrangement events and comparing with cattle chromosomes, which provides a resource for exploring marine mammal adaptation and speciation. We detected a high proportion of long interspersed nuclear elements and expanded gene families, and contraction of major histocompatibility complex region genes which were specific to sperm whale. Using comparisons with sheep and cattle, we analysed positively selected genes to identify gene pathways that may be related to adaptation to the marine environment. Further, we identified possible convergent evolution in aquatic mammals by testing for positively selected genes across three orders of marine mammals. In addition, we used publicly available resequencing data to confirm a rapid decline in global population size in the Pliocene to Pleistocene transition. This study sheds light on the chromosome evolution and genetic mechanisms underpinning sperm whale adaptations, providing valuable resources for future comparative genomics.

Reference

Fan G, Zhang Y, Liu X, et al. The first chromosome - level genome for a marine mammal as a resource to study ecology and evolution[J]. Molecular ecology resources, 2019.

Chromosome level draft genomes of the fall armyworm, *Spodoptera frugiperda* (Lepidoptera: Noctuidae), an alien invasive pest in China

Preprint Publications: [bioRxiv, 2019](#)

Author Affiliation

BGI-Shenzhen | China National GeneBank | Yunnan Agricultural University | Characteristic Agriculture Industry Research Institute, Kunming | Institute of Zoology, Chinese Academy of Sciences, Beijing
MGI, BGI-Shenzhen | BGI-Qingdao | Guangdong Academy of Agricultural Sciences | BGI-Yunnan | Qingdao Agricultural University | Yunnan Plateau Characteristic Agriculture Industry Research Institute
Louisiana State University AgCenter

Abstract

The fall armyworm (FAW), *Spodoptera frugiperda* (J.E. Smith) is a severely destructive pest native to the Americas, but has now become an alien invasive pest in China, and causes significant economic loss. Therefore, in order to make effective management strategies, it is highly essential to understand genomic architecture and its genetic background. In this study, we assembled two chromosome scale genomes of the fall armyworm, representing one male and one female individual procured from Yunnan province of China. The genome sizes were identified as 542.42 Mb with N50 of 14.16 Mb, and 530.77 Mb with N50 of 14.89 Mb for the male and female FAW, respectively. We predicted about 22,201 genes in the male genome. We found the expansion of cytochrome P450 and glutathione s-transferase gene families, which are functionally related to the intensified detoxification and pesticides tolerance. Further population analyses of corn strain (C strain) and rice strain (R strain) revealed that the Chinese fall armyworm was most likely invaded from Africa. These strain information, genome features and possible invasion source described in this study will be extremely important for making effective strategies to manage the fall armyworms.

Reference

Liu H, Lan T, Fang D, et al. Chromosome level draft genomes of the fall armyworm, *Spodoptera frugiperda* (Lepidoptera: Noctuidae), an alien invasive pest in China[J]. *bioRxiv*, 2019: 671560.

Gut microbiome affects the response to anti-PD-1 immunotherapy in patients with hepatocellular carcinoma

Publications: Journal for immunotherapy of cancer, 2019

Author Affiliation

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Shanghai Tenth People's Hospital Affiliated to Tongji University

Abstract

BACKGROUND:

Checkpoint-blockade immunotherapy targeting programmed cell death protein 1 (PD-1) has recently shown promising efficacy in hepatocellular carcinoma (HCC). However, the factors affecting and predicting the response to anti-PD-1 immunotherapy in HCC are still unclear. Herein, we report the dynamic variation characteristics and specificities of the gut microbiome during anti-PD-1 immunotherapy in HCC using metagenomic sequencing.

RESULTS:

Fecal samples from patients responding to immunotherapy showed higher taxa richness and more gene counts than those of non-responders. For dynamic analysis during anti-PD-1 immunotherapy, the dissimilarity of beta diversity became prominent across patients as early as Week 6. In non-responders, Proteobacteria increased from Week 3, and became predominant at Week 12. Twenty responder-enriched species, including *Akkermansia muciniphila* and *Ruminococcaceae* spp., were further identified. The related functional genes and metabolic pathway analysis, such as carbohydrate metabolism and methanogenesis, verified the potential bioactivities of responder-enriched species.

CONCLUSIONS:

Gut microbiome may have a critical impact on the responses of HCC patients treated with anti-PD-1 immunotherapy. The dynamic variation characteristics of the gut microbiome may provide early predictions of the outcomes of immunotherapy in HCC, which is critical for disease-monitoring and treatment decision-making.

Reference

Zheng Y, Wang T, Tu X, et al. Gut microbiome affects the response to anti-PD-1 immunotherapy in patients with hepatocellular carcinoma[J]. Journal for immunotherapy of cancer, 2019, 7(1): 193.

A single bacterium restores the microbiome dysbiosis to protect bones from destruction in a rat model of rheumatoid arthritis

Publications: Microbiome, 2019

Author Affiliation

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Abstract

BACKGROUND:

Early treatment is key for optimizing the therapeutic success of drugs, and the current initiating treatment that blocks the progression of bone destruction during the pre-arthritis stages remains unsatisfactory. The microbial disorder in rheumatoid arthritis (RA) patients is significantly reversed with effective treatment. Modulating aberrant gut microbiomes into a healthy state is a potential therapeutic approach for preventing bone damage.

RESULTS:

By using metagenomic shotgun sequencing and a metagenome-wide association study, we assessed the effect of *Lactobacillus casei* (L. casei) on the induction of arthritis as well as on the associated gut microbiota and immune disorders in adjuvant-induced arthritis (AIA) rats. Treatment of AIA rats with L. casei inhibited joint swelling, lowered arthritis scores, and prevented bone destruction. Along with the relief of arthritis symptoms, dysbiosis in the microbiome of arthritic rats was significantly reduced after L. casei intervention. The relative abundance of AIA-decreased *Lactobacillus* strains, including *Lactobacillus hominis*, *Lactobacillus reuteri*, and *Lactobacillus vaginalis*, were restored to normal and *Lactobacillus acidophilus* was upregulated by the administration of L. casei to the AIA rats. Moreover, L. casei downregulated the expression of pro-inflammatory cytokines, which are closely linked to the effect of the L. casei treatment-associated microbes. Functionally, the maintenance of the redox balance of oxidative stress was involved in the improvement in the L. casei-treated AIA rats.

CONCLUSION:

A single bacterium, L. casei (ATCC334), was able to significantly suppress the induction of AIA and protect bones from destruction in AIA rats by restoring the microbiome dysbiosis in the gut, indicating that using probiotics may be a promising strategy for treating RA, especially in the early stage of the disease.

Reference

Pan H, Guo R, Ju Y, et al. A single bacterium restores the microbiome dysbiosis to protect bones from destruction in a rat model of rheumatoid arthritis[J]. Microbiome, 2019, 7(1): 107.

	Publications	Journal Title	IF	Year	Techology
plant	Modulating plant growth–metabolism coordination for sustainable agriculture	Nature	41.58	2018	RNA-Seq&-ChIP-Seq
human	Methyltransferase SETD2-Mediated Methylation of STAT1 Is Critical for Interferon Antiviral Activity	Cell	30.41	2017	RNA-Seq
human	An Interleukin-25-Mediated Autoregulatory Circuit in Keratinocytes Plays a Pivotal Role in Psoriatic Skin Inflammation	Immunity	22.85	2018	RNA-seq
human	Specific Decrease in B-Cell-Derived Extracellular Vesicles Enhances Post-Chemotherapeutic CD8+ T Cell Responses	Immunity	22.85	2019	RNA-Seq
human	CCR7 Chemokine Receptor-Inducible Inc-Dpf3 Restrains Dendritic Cell Migration by Inhibiting HIF-1 α -Mediated Glycolysis	Immunity	22.85	2019	RNA-Seq
human	A Novel Allosteric Inhibitor of Phosphoglycerate Mutase 1 Suppresses Growth and Metastasis of Non-Small-Cell Lung Cancer	cell metabolism	22.42	2019	RNA-seq
human	Slc6a8-Mediated Creatine Uptake and Accumulation Reprogram Macrophage Polarization via Regulating Cytokine Responses	immunity	21.52	2019	RNA-seq
human	Nutrient Sensing by the Intestinal Epithelium Orchestrates Mucosal Antimicrobial Defense via Translational Control of Hes1	Cell Host & Microbe	17.87	2019	RNA-seq
animal	Precise in vivo genome editing via single homology arm donor mediated intron-targeting gene integration for genetic disease correction	cell research	17.85	2019	RNA-seq
animal	Repopulated microglia are solely derived from the proliferation of residual microglia after acute depletion	Nature Neuroscience	17.84	2018	RNA-Seq
animal	Hyaluronan synthase 2-mediated hyaluronan production mediates Notch1 activation and liver fibrosis	Science Translational Medicine	16.71	2019	RNA-seq
human	Genome-Wide CRISPR-Cas9 Screening Identifies NF- κ B/E2F6 Responsible for EGFRvIII-Associated Temozolomide Resistance in Glioblastoma	Advanced Science	15.80	2019	RNA-seq
animal	The CRISPR-Cas13a Gene-Editing System Induces Collateral Cleavage of RNA in Glioma Cells	advanced Science	15.804	2019	RNA-seq
animal	KRAB-type zinc-finger proteins PITA and PISA specifically regulate p53-dependent glycolysis and mitochondrial respiration	Cell research	15.61	2018	RNA-seq
animal	Pioneering function of Isl1 in the epigenetic control of cardiomyocyte cell fate	Cell research	15.39	2019	RNA-Seq
human	Hepatocyte TRAF6 Aggravates Hepatic Inflammation and Fibrosis by Promoting Lys6- Linked Polyubiquitination of ASK1	hepatology	14.97	2019	RNA-seq
human	Landscape of Intercellular Crosstalk in Healthy and NASH Liver Revealed by Single-Cell Secretome Gene Analysis	molecular cell	14.55	2019	RNA-seq
human	Glutarylation of Histone H4 Lysine 91 Regulates Chromatin Dynamics	molecular cell	14.55	2019	RNA-seq
animal	Menin Deficiency Leads to Depressive-like Behaviors in Mice by Modulating Astrocyte-Mediated Neuroinflammation	Neuron	14.32	2018	RNA-Seq
human	Nucleoporin Seh1 Interacts with Olig2/Brd7 to Promote Oligodendrocyte Differentiation and Myelination	Neuron	14.32	2019	RNA-seq
microor-ganism	Enterovirus pathogenesis requires the host methyltransferase SETD3	Nature Microbiology	14.30	2019	RNA-seq
microor-ganism	Host serum iron modulates dengue virus acquisition by mosquitoes	Nature Microbiology	14.30	2019	RNA-seq
human	Breast milk alkylglycerols sustain beige adipocytes through adipose tissue macrophages	JOURNAL OF CLINICAL INVESTIGATION	13.25	2019	RNA-seq
animal	Hepatic IRF6 alleviates liver steatosis and metabolic disorder by transcriptionally suppressing PPAR γ	hepatology	13.25	2019	RNA-Seq&ChIP-Seq
animal	Integrated Omics Reveals Tollip as an Aggravator and Therapeutic Target for Hepatic Ischemia-Reperfusion Injury in Mice	hepatology	13.25	2019	RNA-seq

	Publications	Journal Title	IF	Year	Techology
animal	Hepatic Interferon Regulatory Factor 6 Alleviates Liver Steatosis and Metabolic Disorder by Transcriptionally Suppressing Peroxisome Proliferator-Activated Receptor γ in Mice	hepatology	13.25	2019	RNA-seq
human	Translation of the circular RNA circ β -catenin promotes liver cancer cell growth through activation of the Wnt pathway	Genome Biology	13.21	2019	RNA-seq
animal	Glucocorticoid receptor in stromal cells is essential for glucocorticoid-mediated suppression of inflammation in arthritis	Annals of the Rheumatic Diseases	12.38	2018	RNA-Seq
human	Salt-inducible kinases dictate parathyroid hormone receptor action in bone development and remodeling	JOURNAL OF CLINICAL INVESTIGATION	12.28	2019	RNA-seq
plant	Hydrogen peroxide positively regulates brassinosteroid signaling through oxidation of the BRASSI-NAZOLE-RESISTANT1 transcription factor	Nature Communications	12.12	2018	RNA-seq
human	STAG2 deficiency induces interferon responses via cGAS-STING pathway and restricts virus infection	Nature Communications	12.12	2018	RNA-seq
human	Mutually exclusive acetylation and ubiquitylation of the splicing factor SRSF5 control tumor growth	Nature Communications	12.12	2018	RNA-Seq
human	Precisely controlling endogenous protein dosage in hPSCs and derivatives to model FOXG1 syndrome	Nature Communications	12.12	2019	RNA-Seq
animal	Primary cilia regulate hematopoietic stem and progenitor cell specification through Notch signaling in zebrafish	Nature Communications	12.12	2019	RNA-seq
human	Fas signaling-mediated TH9 cell differentiation favors bowel inflammation and antitumor functions	Nature Communications	11.88	2019	RNA-seq
animal	Pioneer and repressive functions of p63 during zebrafish embryonic ectoderm specification	Nature Communications	11.88	2019	RNA-seq
human	UHRF1 suppresses retrotransposons and cooperates with PRMT5 and PIWI proteins in male germ cells	nature communications	11.88	2019	RNA-seq
animal	Activation of P-TEFb by cAMP-PKA signaling in autosomal dominant polycystic kidney disease	Science Advances	11.51	2019	RNA-Seq&-ChIP-Seq
human	Glutamylation of deubiquitinase BAP1 controls self-renewal of hematopoietic stem cells and hematopoiesis	JOURNAL OF EXPERIMENTAL MEDICINE	10.892	2019	RNA-seq
human	The E3 ligase VHL promotes follicular helper T cell differentiation via glycolytic-epigenetic control	JOURNAL OF EXPERIMENTAL MEDICINE	10.79	2019	RNA-seq
animal	Comprehensive transcriptomic view of the role of the LGALS12 gene in porcine subcutaneous and intramuscular adipocytes	Molecular Cancer	10.68	2019	RNA-seq
human	Diminished OPA1 expression and impaired mitochondrial morphology and homeostasis in Aprataxin-deficient cells	Nucleic Acids Research	10.16	2019	RNA-Seq
animal	Organic cation transporter 3 (Oct3) is a distinct catecholamines clearance route in adipocytes mediating the beiging of white adipose tissue	PLOS BIOL	9.80	2019	RNA-Seq
animal	Nuclear carbonic anhydrase 6B associates with PRMT5 to epigenetically promote IL-12 expression in innate response	PNAS	9.66	2017	RNA-Seq&-ChIP-Seq
human	Roles of the CSE1L-mediated nuclear import pathway in epigenetic silencing	PNAS	9.66	2018	RNA-seq
animal	Knockout of juvenile hormone receptor, Methoprene-tolerant, induces black larval phenotype in the yellow fever mosquito, <i>Aedes aegypti</i>	PNAS	9.58	2019	RNA-seq
microorganism	Rapid pathway prototyping and engineering using in vitro and in vivo synthetic genome SCRaMbLE-in methods	Nature Communications	12.12	2018	WGS
plant	Resequencing 545 ginkgo genomes across the world reveals the evolutionary history of the living fossil	Nature Communications	11.88	2019	WGS
0	Lamin A/C promotes DNA base excision repair	Nucleic Acids Research	11.15	2019	WGS
animal	The first chromosome-level genome for a marine mammal as a resource to study ecology and evolution	Molecular Ecology Resources	7.33	2019	WGS

	Publications	Journal Title	IF	Year	Techology
human	A reference human genome dataset of the BGISEQ-500 sequencer	GigaScience	7.27	2017	WGS
animal	Comparative performance of the BGISEQ-500 versus Illumina HiSeq2500 sequencing platforms for palaeogenomic sequencing	GigaScience	7.27	2017	WGS
plant	Molecular digitization of a botanical garden: high-depth whole genome sequencing of 689 vascular plant species from the Ruili Botanical Garden	GigaScience	7.27	2019	WGS
animal	The Marine Mammal Class II Major Histocompatibility Complex Organization	Frontiers in Immunology	6.43	2019	WGS
human	C/EBP β enhances platinum resistance of ovarian cancer cells by reprogramming H3K79 methylation	Nature Communications	12.12	2018	WES
human	Epigenetic alterations are associated with tumor mutation burden in non-small cell lung cancer	Journal for Immuno Therapy of Cancer	8.68	2019	WES
human	Engineering Forward Genetics into Cultured Cancer Cells for Chemical Target Identification	cell chemical biology	6.76	2019	WES
human	Whole exome sequencing reveals HSPA1L as a genetic risk factor for spontaneous preterm birth	PLOS.Genetics	5.54	2018	WES
animal	Dissecting primate early post-implantation development using long-term in vitro embryo culture	science	41.037	2019	scRNA-Seq & scATAC-seq
animal	Comparative analysis of sequencing technologies platforms for single-cell transcriptomics	GENOME BIOLOGY	13.21	2019	scRNA-Seq
human	An integrated chromatin accessibility and transcriptome landscape of human pre-implantation embryos	Nature Communications	12.12	2019	ATAC-seq & LICAT-seq
human	Deconvolution of single-cell multi-omics layers reveals regulatory heterogeneity	Nature Communications	12.12	2019	scCAT-seq
human	Efficient and unique co-barcoding of second-generation sequencing reads from long DNA molecules enabling cost effective and accurate sequencing, haplotyping, and de novo assembly	GENOME RESEARCH	11.92	2019	stLFR
animal	Chromosome-level reference genome of the Siamese fighting fish <i>Betta splendens</i> , a model species for the study of aggression	GigaScience	7.27	2018	Hi-C library
human	Single-cell transcriptomic landscape of nucleated cells in umbilical cord blood	GigaScience	7.27	2019	scRNA-Seq
animal	Dean flow assisted single cell and bead encapsulation for high performance single cell expression profiling	ACS Sensors	5.71	2019	scRNA-Seq
animal	An ATAC-seq atlas of chromatin accessibility in mouse tissues	Scientific Data	5.31	2019	ATAC-seq
animal	Systematic evaluation of <i>C. elegans</i> lincRNAs with CRISPR knockout mutants	Genome Biology	13.21	2019	lncRNA
human	The FOXN3-NEAT1-SIN3A repressor complex promotes progression of hormonally responsive breast cancer	The Journal of Clinical Investigation	12.78	2017	ChIP-Seq
microorganism	Altered respiratory virome and serum cytokine profile associated with recurrent respiratory tract infections in children	Nature Communications	12.12	2019	Pathogen detection
microorganism	A single bacterium restores the microbiome dysbiosis to protect bones from destruction in a rat model of rheumatoid arthritis	Microbiome	10.47	2019	metagenome
human	Low-pass genome sequencing versus chromosomal microarray analysis: implementation in prenatal diagnosis	genetics in medicine	8.683	2019	CNV-seq
microorganism	Gut microbiome affects the response to anti-PD-1 immunotherapy in patients with hepatocellular carcinoma	Journal for Immuno Therapy of Cancer	8.68	2019	metagenome
human	Advanced Whole-Genome Sequencing and Analysis of Fetal Genomes from Amniotic Fluid	Clinical Chemistry	8.64	2018	PGS
microorganism	A novel affordable reagent for room temperature storage and transport of fecal samples for metagenomic analyses	Microbiome	8.50	2018	metagenome
human	Generation of Highly Biomimetic Quality Control Materials for Noninvasive Prenatal Testing Based on Enzymatic Digestion of Matched Mother-Child Cell Lines	CLINICAL CHEMISTRY	8.01	2019	NIFTY

	Publications	Journal Title	IF	Year	Techology
human	Ai-lncRNA EGOT enhancing autophagy sensitizes paclitaxel cytotoxicity via upregulation of ITPR1 expression by RNA-RNA and RNA-protein interactions in human cancer	Molecular Cancer	7.78	2019	ChIP-seq
microor-ganism	High - throughput identification and diagnostics of pathogens and pests: Overview and practical recommendations	Molecular Ecology Resources	7.33	2018	Pathogen detection
human	Assessment of the cPAS-based BGISEQ-500 platform for metagenomic sequencing	GigaScience	7.27	2017	metagenome
animal	A gene catalogue of the Sprague-Dawley rat gut metagenome	GigaScience	7.27	2018	metagenome
human	The metagenome of the female upper reproductive tract	GigaScience	7.27	2018	metagenome
plant	Prospects and challenges of implementing DNA metabarcoding for high-throughput insect surveillance	GigaScience	7.27	2019	review
microor-ganism	Tamdy Virus in Ixodid Ticks Infesting Bactrian Camels,Xinjiang, China, 2018	Emerging Infectious Diseases	7.19	2019	Pathogen detection
microor-ganism	Distinct gut metagenomics and metaproteomics signatures in prediabetics and treatment-naïve type 2 diabetics	EBioMedicine	6.68	2019	metagenome
human	Development of coupling controlled polymerizations by adapter-ligation in mate-pair sequencing for detection of various genomic variants in one single assay	DNA RESEARCH	5.42	2019	long mate pair library
human	M7 - FLIPI is not prognostic in follicular lymphoma patients with first - line rituximab chemo - free therapy	British Journal of Haematology	5.21	2019	capture
microor-ganism	Incremental value of metagenomic next generation sequencing for the diagnosis of suspected focal infection in adults	Journal of Infection	5.10	2019	Pathogen detection
human	Development and comprehensive evaluation of a noninvasive prenatal paternity testing method through a scaled trial	Forensic Science International-Genetics	4.88	2019	NIPPT
human	A reference system for BRCA mutation detection based on next-generation sequencing in the Chinese population	JOURNAL OF MOLECULAR DIAGNOSTICS	4.88	2019	capture
human	Validation of combinatorial probe-anchor ligation-based sequencing as non-invasive prenatal test for trisomy at a central laboratory	Ultrasound in Obstetrics & Gynecology	4.71	2017	NIFTY
animal	High-coverage genomes to elucidate the evolution of penguins	GigaScience	4.69	2019	10X Genomics genomic libraries
animal	Aberrantly expressed long non - coding RNAs in air pollution - induced congenital defects	JOURNAL OF CELLULAR AND MOLECULAR MEDICINE	4.66	2019	lncRNA
microor-ganism	Diminishing microbiome richness and distinction in the lower respiratory tract of lung cancer patients: a multiple comparative study design with independent validation	Lung Cancer	4.60	2019	metagenome
microor-ganism	The Feasibility of Metagenomic Next-Generation Sequencing to Identify Pathogens Causing Tuberculous Meningitis in Cerebrospinal Fluid	Frontiers in Microbiology	4.259	2019	Pathogen detection
microor-ganism	Current Status and Potential Applications of Underexplored Prokaryotes	Microorganisms	4.17	2019	metagenome
microor-ganism	Taxonomic and Functional Characterization of the Microbial Community During Spontaneous in vitro Fermentation of Riesling Must	Frontiers in Microbiology	4.08	2019	metagenome
microor-ganism	Genome comparison of African swine fever virus China/2018/AnhuiXCGQ strain and related European p72 Genotype II strains	TRANSBOUND EMERG DIS	3.59	2019	Pathogen detection
microor-ganism	Value of mNGS in sonication fluid for the diagnosis of periprosthetic joint infection	JOURNAL OF ARTHROPLASTY	3.524	2019	Pathogen detection
human	Prenatal Diagnosis of Fetuses with Increased Nuchal Translucency by Genome Sequencing Analysis	Frontiers in Genetics	3.52	2019	CNV-seq
plant	mTERF5 Acts as a Transcriptional Pausing Factor to Positively Regulate Transcription of Chloroplast psbEFLJ	molecular plant	9.33	2019	RNA-seq



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