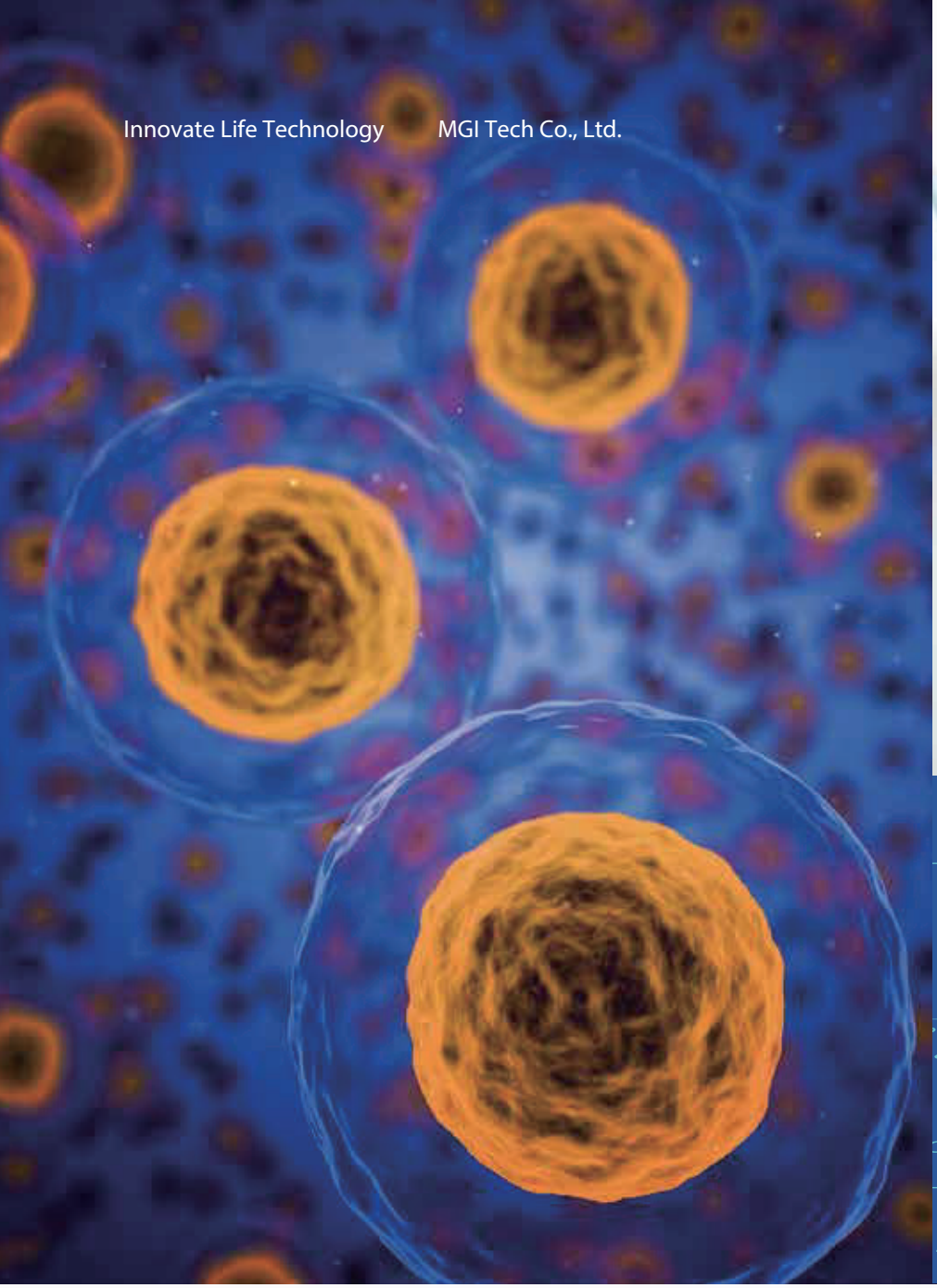
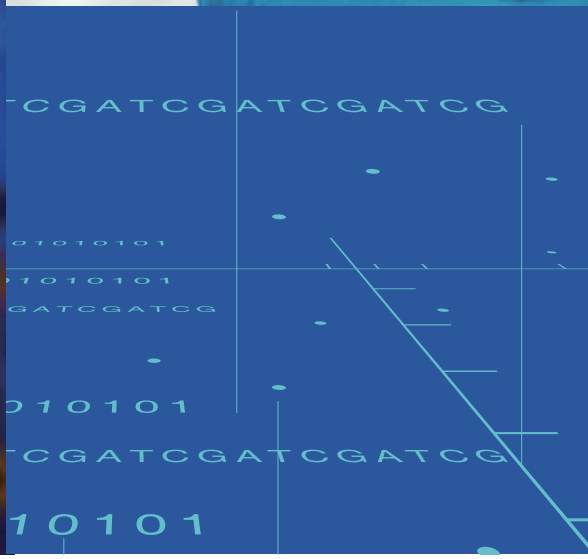
Innovate Life Technology MGI Tech Co., Ltd.





Microbial Detection Total Solution

MGI sequencing platform for pathogen fast identification

About us

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 39 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.

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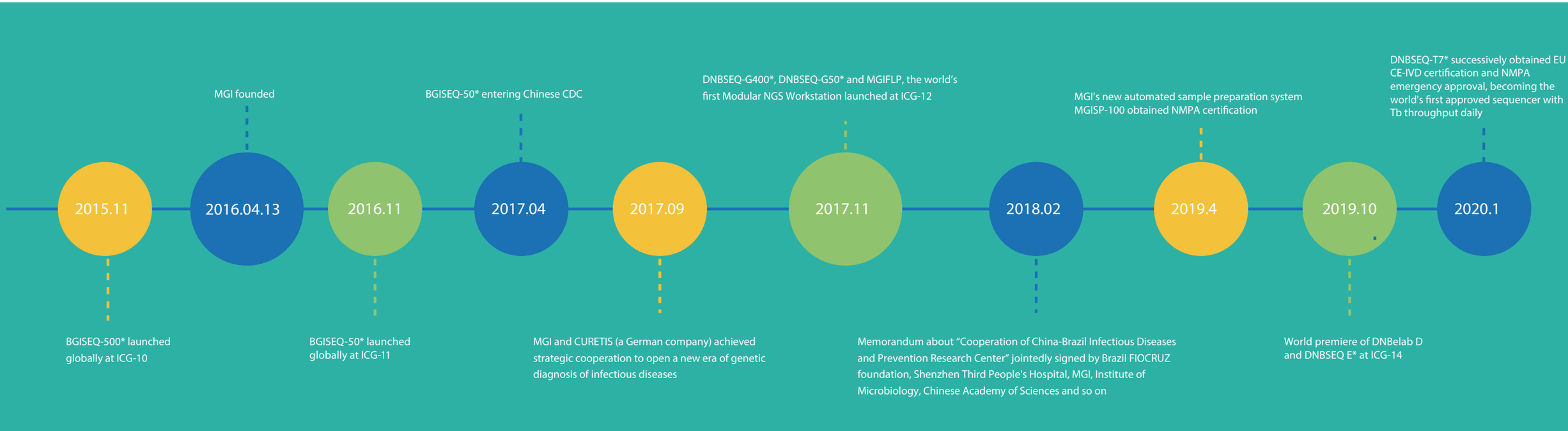
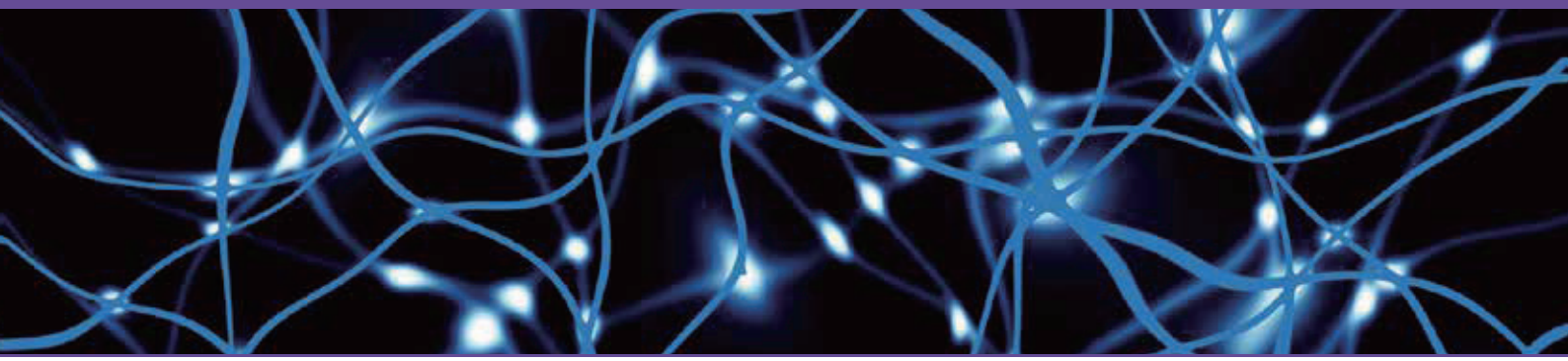
Timeline of MGI Microbial Solutions



Overview



- How to identify the pathogen that leads to infectious disease ?

Identification of pathogens is essential in the treatment of patients with infectious diseases. Currently, the predominant techniques rely on conventional microbiology approaches. However, traditional methods often fail to identify mixed-pathogens in complex clinical samples, making the diagnosis and treatment of infection more challenging. Therefore, a rapid and precise pathogen detection approach is important to understand and treat the infection.

- The challenge of applying High-throughput sequencing technology to pathogen detection

High-throughput sequencing technology empowers the large-scale pathogen screening by generating large amounts of genomics data. However, the tremendous amount of raw information requires a well-built database and efficient analysis tools to support accurate identification.

- MGI sequencing technology for pathogen detection

MGI has developed a high-throughput sequencing platform integrated with a pathogen detection system. This innovative technology can perform fast, accurate and comprehensive pathogen screening for clinical diagnosis. Moreover, MGI provides varies hardware devices and compatible reagent kits for the system to support an extensive range of pathogen testing.

Traditional pathogen detection methods

Culture-based method

Laborious, time-consuming.
Not suitable for unculturable pathogens.
Few positive results.

TOF-MS (Time-of-flight mass spectrometry)

Need clonal isolates.

Immunoassay

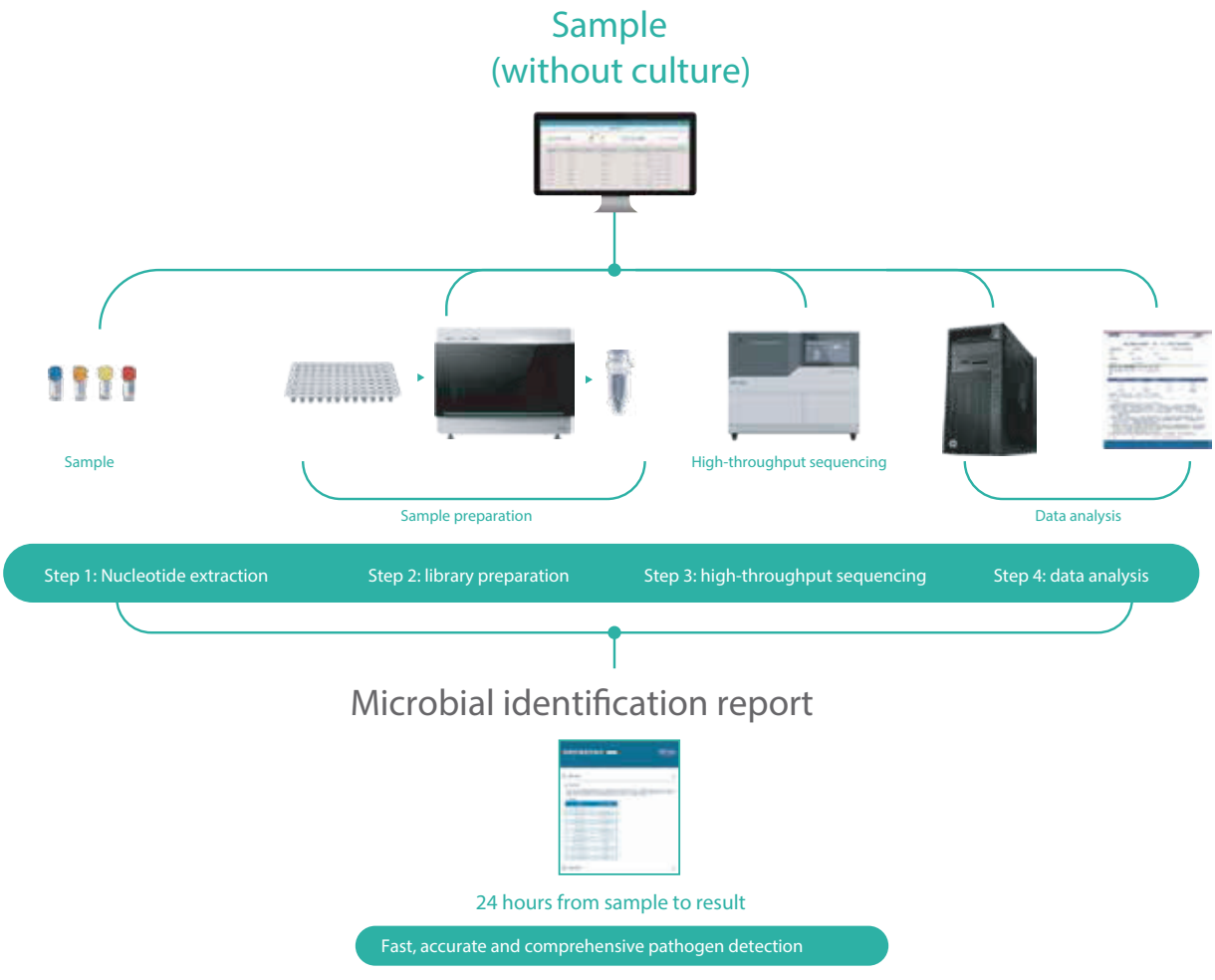
Sensitivity and specificity issues.

PCR screening

Can only detect known pathogens and prone to assay specific limitations.

Each method has its limitation and can only detect known pathogens.

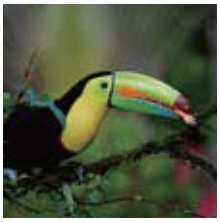
MGI sequencing approach



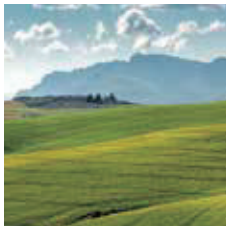
Applications

MGI Microbiology Detection Total Solution supports massive screening on unknown pathogens in human or animal infection and allows accurate diagnosis and treatment. Its diverse applications are listed below:

Animal health

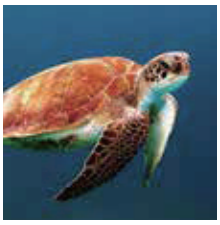


Agriculture

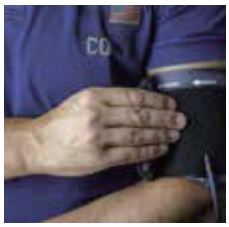


Travel health

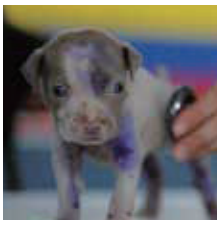
Animal science and medicine



Public health



Prevention and control of human and animal diseases



Food safety

Public healthcare

Precision medicine

The MGI High-throughput Sequencing Platform Allows Detection of

Unculturable pathogens | Pathogens without time-consuming culture | Co-infection

Infection of a rare or new pathogen strain | Hard-to-detect dysbacteriosis

MGI Microbiology DetectionTotal Solution is based on the data produced by an autonomous high-throughput sequencing platform, an automated sample preparation system and a self-developed supporting reagent, and is combined with an independently developed rapid identification system for pathogenic infections, perfectly realizing rapid, accurate and comprehensive identification of microorganisms.

Our Advantages

MGI Microbiology DetectionTotal Solution is mainly for unexplained infections to carry out broad-spectrum pathogen microbiological screening, to help users quickly, accurately and comprehensive microbial classification identification, so that high-throughput sequencing technology can be used in the diagnosis and treatment of infectious diseases at their fingertips.

Independent platforms

Fully-automated sample preparation system, high-throughput sequencing platform and various compatible reagent kits.

Up-to-date microbial database

A comprehensive database of more than 20, 000 microbial genomics enabling massive screening at one time.

Streamlined workflow

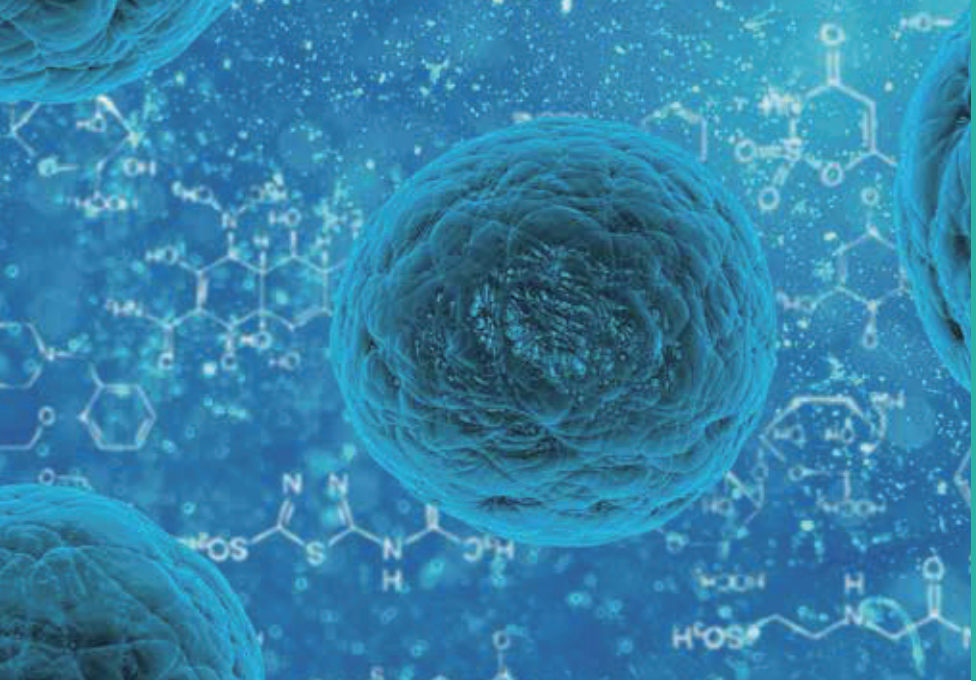
24 hours from sample to result with one-stop solution.

No need for preliminary test

No culture needed. Solutions for a wide variety of environmental or clinical samples (human or animal blood, respiratory tract fluid, cerebrospinal fluid and intestine).

On-board analysis system

Reliable data analysis at both nucleic acid and protein levels.



MGI's microbial detection total solution is based on the data generated by independent high-throughput sequencing platform, automated sample preparation system, self-developed compatible reagents, and self-developed rapid identification system for pathogen infection, which could realize fast, accurate and comprehensive microbial detection.

Independently developed platforms

MGI's fully-integrated sequencing system enables high-throughput sequencing technology to support the real-time diagnosis of infectious diseases.

▶ Genetic Sequencer

Product Information				
Product Model	DNBSEQ-G50	DNBSEQ-G400FAST*	DNBSEQ-G400	DNBSEQ-T7
Product Feature	Efficient	Fast	Adpative	Ultra-high Throughput
Flow cell Type	FCS&FCL	FCS	FCS&FCL	FC
LANE/Flow Cell	1 LANE	2 LANE	2 or 4 LANE	1 LANE
Operation Mode	Medium Throughput	Medium Throughput	High Throughput	Ultra-high Throughput
Max. Throughput/RUN	150 GB	330 GB	1440 GB	6 TB
Effective Reads/Flow Cell	500 M/100 M	550 M	1500 M-1800 M	5000 M
Average Run Time	9-40 h	13-37 h	FCS: 13-37 h FCL: 14-109 h	24-30 h
Min. Read Length	SE50	SE100	SE50	PE100
Max. Read Length	PE150	PE150	SE400/PE200	PE150

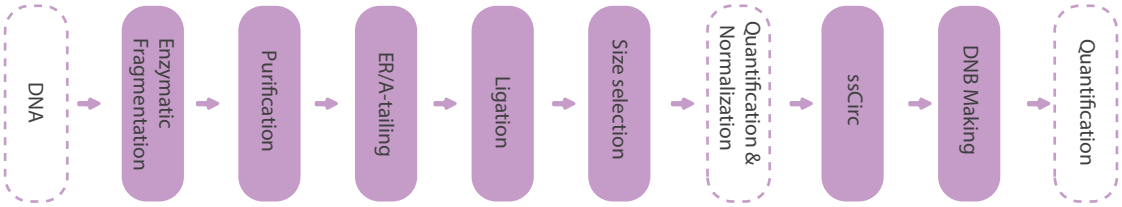
Automated sample preparation system

MGISP-100/MGISP-960 automated sample preparation system integrated 8/96 channel pipette, as automated workstations specialized for high-throughput sequencing library preparation.

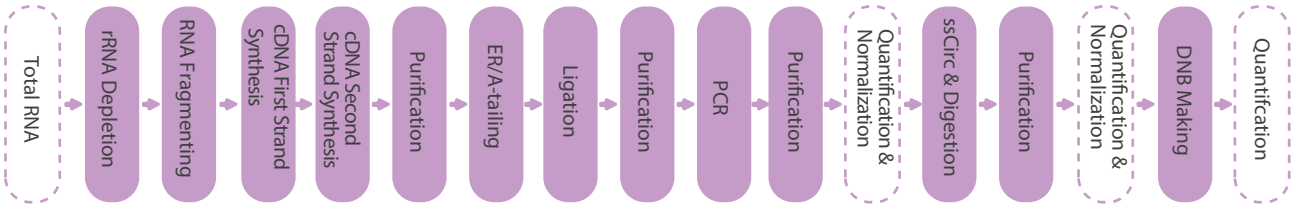
Certification:
NMPA, CE, CB, CTUVUS
Throughput:
16 samples/run

Certification:
NMPA, CE, CB, CTUVUS
Throughput;
96 samples/run

WGS Library Preparation



RNAseq Library Preparation



Pathogen Fast Identification System

MGI has developed a database containing the genetic information of >20, 000 microbes and software for PFI(Pathogen Fast Identification). The integrated system can quickly generate reliable analyses of microbial genome information and the identification report automatically.

Product features

Simple workflow

The instrument has automatic analysis software to launch data analysis and FASTQ files which are compatible for secondary analysis.

Species coverage

In addition to human reference genome sequence, the system collects information about common animal reference sequences such as pig, goat, sheep, mice, rat, carp, goose, chicken, duck, cow, cat, dog and rabbit. The feature enables comprehensive analysis to identify host species.

Comprehensive analysis

MGI sequencers eliminate high background or noisy sequencing signal to generate highly accurate pathogen identification using RNA transcriptome and DNA genomic sequencing.

Product introduction

MGI-developed pathogen fast identification system, known as PFI (Pathogen Fast Identification), is a software-and-hardware combination solution, Including a microbial database with analytical processes, and full process management of sample input and report output via ZLIMS, with the complete system loaded onto the bioinformatics hardware acceleration system server.

The server

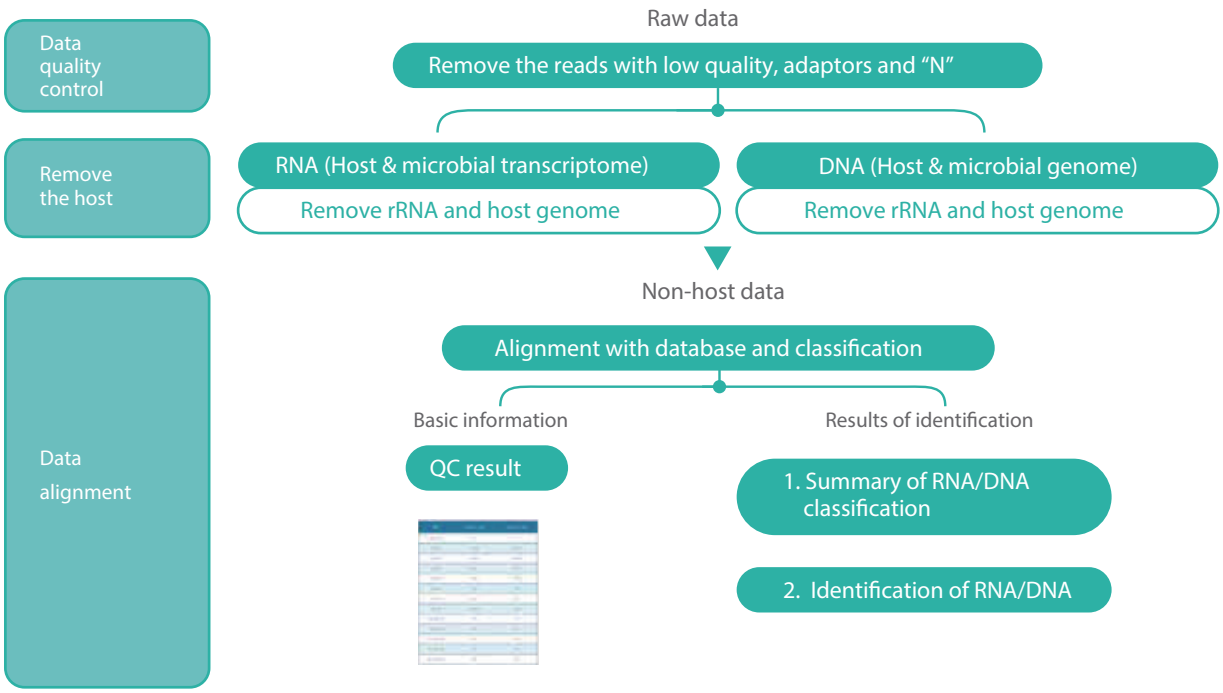
With the HP Z8G4 workstation, the stability and reliability are strong.
CPU: Intel Xeon 6240×2 | Memory: 192GB DDR4 | SSD: 2TB plus 250GB | Mechanical Drive: 30TB 7200 | SATA 3.5 inch

Database

The pathogen fast identification system collects more than 20,000 microbial genomic sequences (if the species has multiple reference genomes, the information will also be included) in the database which supports rapid and precise detection.

Microbial classification	Species	Genus
Bacteria	7000+	1900+
Archaea	300+	100+
Viruses	9000+	2500+
Fungi	8000+	1000+
Parasites	100+	50+

Workflow



ZLIMS

ZLIMS, a MGI laboratory information management software, supports tracking sequencing runs, data generation and management. The pathogen fast identification system integrates onboard ZLIMS to monitor run progress of sample collection, library preparation, sequencing and launch automated data analysis.

- Manage the details of each experiment step
- Manage the priority of each workflow
- Effectively schedule all resources
- Monitor sequencing quality and instrument information in real-time
- Trace the whole workflow of experimental data
- Support all kinds of biological information analysis process and report

Our Solution

MGI microbial detection total solution does not require sample culture and preliminary tests . Additionally, it can identify microorganisms in environmental or clinical samples at one stop.

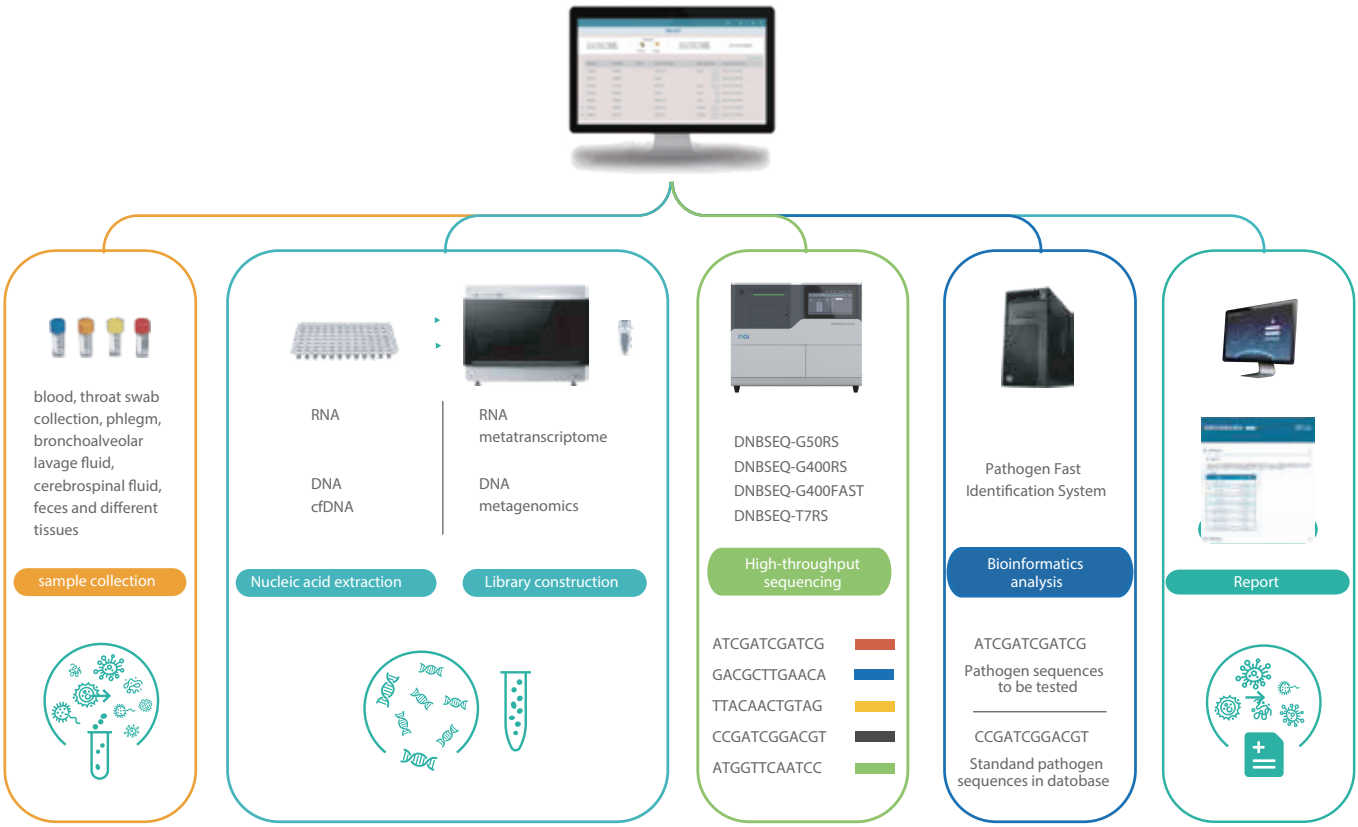
1 Sample Collection And Accession

2 Nucleic Acid Extraction And Library Preparation

3 Sequencing And Base-calling

4 Bioinformatics Analysis

5 Report



The MGI pathogen fast identification system is highly versatile, providing solutions for a broad range of detection with the customized panel at one stop.

Automatic operation solution

Simple and Efficient

Offers the pathogen fast identification of various DNA/RNA sample from blood, throat swab collection, phlegm, bronchoalveolar lavage fluid, cerebrospinal fluid, feces and different tissues. Fully-automated system provides a fast, convenient and efficient user experience for pathogen detection.

▶ Step 1
Nucleic acid extraction

▶ Step 2
Library construction

▶ Step 3
High-throughput sequencing

▶ Step 4
Bioinformatics analysis

Sample source

Plasma/Blood/ throat swab collection, phlegm, bronchoa--lveolar lavage fluid, cerebrospinal fluid, feces and different tissues

Nucleic acid source

cfDNA or 150-250bp fragmented DNA

gDNA (enzymatic fragmentation)

Total RNA

MGISP-100

Library construction kit

MGIEasy Cell-free DNA Library Prep Set

MGIEasy FS DNA Library Prep Set

MGIEasy RNA Library Prep Set

MGISP-960

DNBSEQ-G50RS

DNBSEQ-G400FAST

DNBSEQ-G400RS

DNBSEQ-T7RS

High-throughput sequencing

DNBSEQ-G50RS High-throughput Sequencing Set
DNBSEQ-G400RS High-throughput Sequencing Set
DNBSEQ-G400RS High-throughput Rapid Sequencing Set
DNBSEQ-T7RS High-throughput Sequencing Set

Analysis server of bioinformatics

Analysis software

Pathogen Fast Identification System

Hands on time

Automatic time

Our Report

The MGI sequencer automatically generates pathogen detection report in a short time including two main sections :

▶ General information

The system automatically removes low-quality host/rRNA sequence in raw data and calculates clean reads and qualified data.

▶ Identification result

The system initially analyzes DNA/RNA level by comparing the sample sequencing information to the database of bacterial, viral, archaeal, fungal and parasite genomes. Subsequently it gener - ates a pathogen identification report shown as the Venn diagram. The report includes both DNA and RNA identification result and comparison of DNA versus RNA result.

2.1 Summary	2.2 DNA/RNA identification
2.3 Toxicity identification	2.4 Identification of resistance genes

Case Study

The microbial detection total solution is to understand the diversity within samples by sequencing all nucleotides of both host and microbes. This method does not require preliminary knowledge of pathogenic microbial genomes and as such, can identify unknown pathogens in infectious disease. Importantly, the unique identification technique supports developing strategies to control and prevent human and animal infectious diseases.

Case 1 The prevention and control of Corona Virus Disease 2019（COVID-19）

Overview

With the Corona Virus Disease 2019（COVID-19）entering the stage of attack, nucleic acid detection technology based on RT-PCR played an important role in the rapid identification and diagnosis of the SARS-CoV-2 virus. However, to study the origin, variation evolution and pathogenic mechanism of the SARS-CoV-2 virus, it is necessary to obtain complete viral genome information, which depends on high-throughput sequencing and viral sequence assembly.

A suspected sample of the COVID-19 received by a CDC was detected as an example, to analyze the Metatranscriptomic Sequencing and virus sequence assembly process of the SARS-CoV-2 virus that is from the respiratory sample of the CDC's first case.

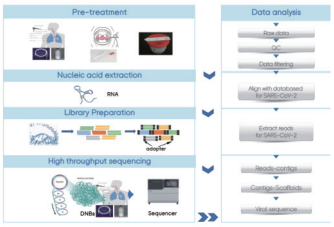


Figure 1-1 Whole process of identification and assembly the whole genome sequence of COVID-19 (SARS-CoV-2).

Solution

At January 20th, Library Prearation was construct using MGIEasy RNA library preparation reagent kit, making DNA nanoballs.
At January 21st, basted on the DNBSEQ-G50 platform, high-depth sequencing with 300 M reads were performed on the respiratory samples of the first case reported in the region. The sequencing scheme was SE100.
At January 22nd, combined with the MGI Pathogen Fast Identification (PFI) software, SARS-CoV-2 reads were identified, and the IDBA method with high assembly efficiency was used to obtain the full-length genome sequence (Figure 1-1).

Table 1-1 Top 10 virus species identification summary table of PFI report

No.	Species Scientific Name	Reads Number	Relative Abundance (%)
1	SARS-CoV-2	2,337442	60.685
2	Proteus phage VB PmiS-Isfahan	3,344	0.087
3	Parvovirus NIH-CQV	203	0.005
4	Severe acute respiratorysyndrome-related coronavirus	140	0.004
5	Uncultured crAssphage	64	0.002
6	Bat coronavirus BM48-31/BGR/2008	43	0.001
7	Staphylococcus virus IPLA5	42	0.001
8	Rhodoferax phage P26218	41	0.001
9	Acanthamoeba polyphaga moumouvirus	34	8.827e-04
10	Megavirus chilensis	22	5.712e-04

Result

After sequencing, DNBSEQ-G50 sequencer generated 32 Gb data with a total of 318 M metagenomesequencing reads. Combined with the Pathogen Fast Identification software, a total of 2,337,442 SARS-CoV-2 reads were identified (Table 1-1). The analysis software automatically extracted the reads of SARS-CoV-2 from all the sequences. The IDBA method with high assembly efficiency was used, and a full-length 29.9kb genome sequence was obtained (Figure 1-2).

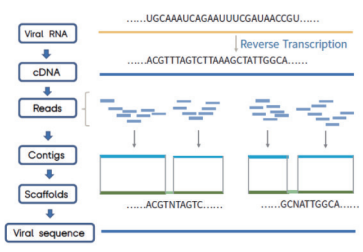
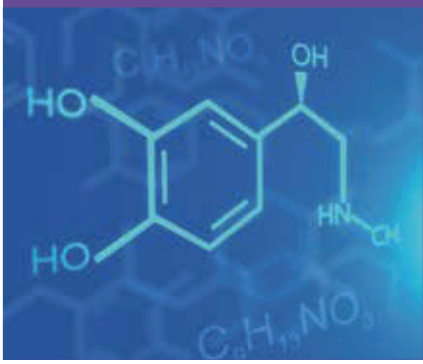


Figure 1-2 Assembly process of viral genome sequences

Paper

A novel Enterovirus 96 circulating in China causes hand, foot, and mouth disease published on Virus Genes on February 7th, 2017



Case 2 Research of SARS-CoV-2

Overview

Understanding the evolution and transmission patterns of a virus after it enters a new population is crucial for designing effective strategies for disease control and prevention. Researchers generated virus genome sequences form 53 patients in a certain province using both metagenomic sequencing and multiplex PCR amplification followed by sequencing and combined genetic and epidemiological data to investigate the genetic diversity, evolution, and epidemiology of SARS-CoV-2.

Solution

DNA-depleted and purified RNA was used to construct the single-stranded circular DNA library with MGIEasy RNA Library preparation reagent set following manufacturer's protocol. Finally, 60fmol of PCR products were Unique Dual Indexed (UDI), circularized, and amplified by rolling circle replication (RCR) to generate DNA nanoball (DNBs)-based libraries. DNBs preps of clinical samples were sequenced on the MGISEQ-2000 platform.

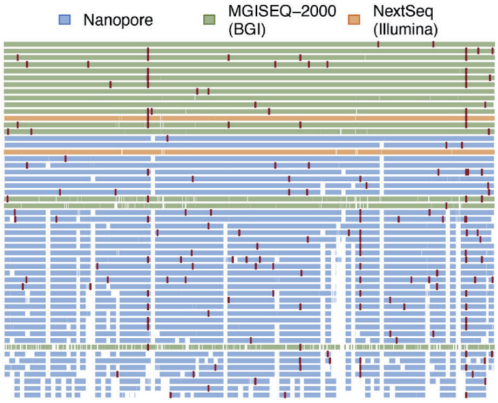


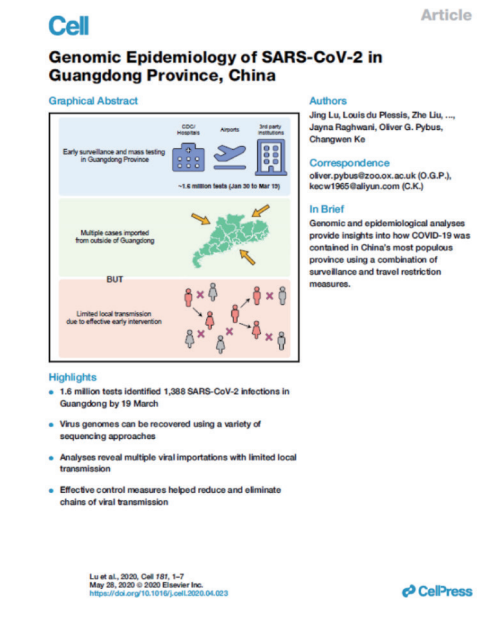
Figure 2-1 Genome coverage map for the 53 genomes reported here, ordered by%genome coverage. Single nucleotide polymorphisms (with respect to the reference genome MN908947.3) are colored in red. Each genome is colored according to the sequencing approach used.

Result

After assembling, 53 full length genome of SARS-CoV-2 were generated. It was found that under the same CT value, the genome data of SARS-CoV-2 generated by metagenomic sequencing on MGI's high-throughput sequencing platform could be more easily splice and assembled into a complete genome(Figure 2-1).

Paper

Genomic epidemiology of SARS-CoV-2 in Guangdong Province, China.
Published on Cell in April 2020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Article

Genomic Epidemiology of SARS-CoV-2 in Guangdong Province, China

Graphical Abstract

Authors

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In Brief

Genomic and epidemiological analyses provide insights into how COVID-19 was contained in China's most populous province using a combination of surveillance and travel restriction measures.

Highlights

- 1.6 million tests identified 1,388 SARS-CoV-2 infections in Guangdong by 19 March
- Virus genomes can be recovered using a variety of sequencing approaches
- Analyses reveal multiple viral importations with limited local transmission
- Effective control measures helped reduce and eliminate chains of viral transmission

Lu et al., 2020, Cell 181, 1–7
May 28, 2020 © 2020 Elsevier Inc.
https://doi.org/10.1016/j.cell.2020.04.023

CellPress

Case 3 Diagnosis of rare pathogen

Overview

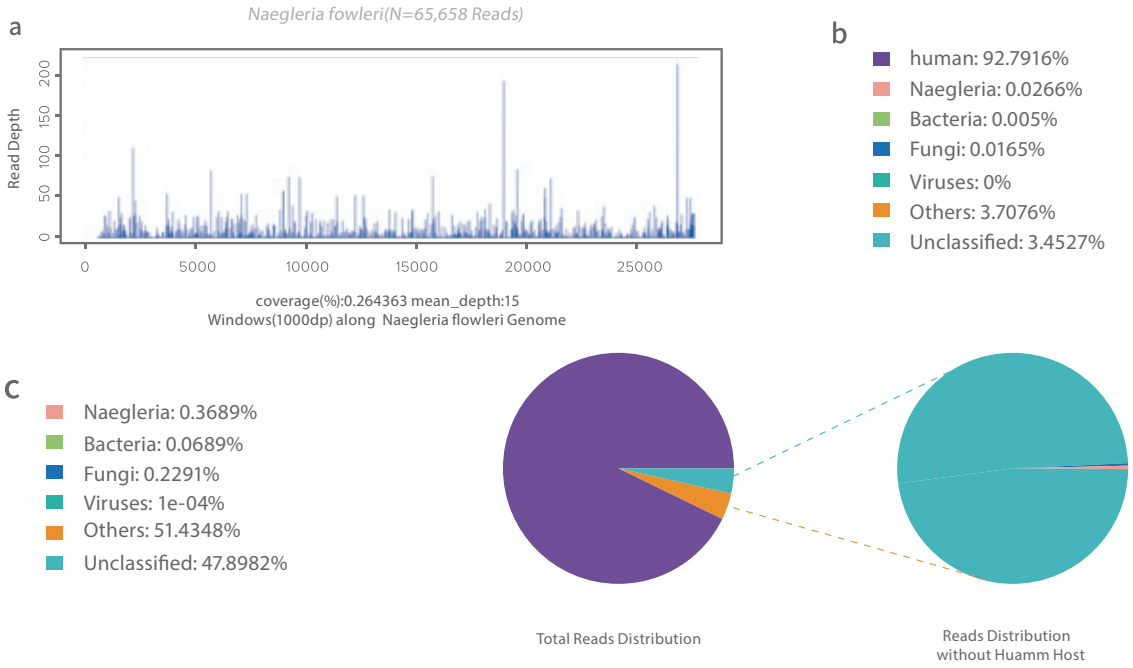
On August 20, 2018, A 42-year-old man was hospitalized after presenting with symptoms of severe headache, fever of 38.4 °C, and elevated CSF leukocyte and protein levels. 24 hours post-pre - sentation, the patient spoke incoherently, had breathing difficulties, became comatose and was subsequently transferred to ICU.
Further examination by CT scan showed hydrocephalus and brain edema. Four days later, a culture from cerebrospinal fluid samples showed negative results for bacteria and fungi, therefore, to identify the pathogen, the sample was further analyzed using high-throughput sequencing on August 31. Results were reported to clinicians 2 days later.

Solution

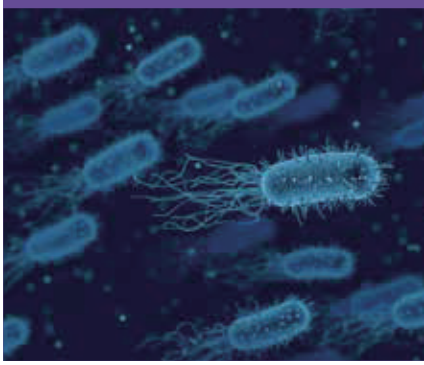
The cerebrospinal fluid sample collected from the patient was analyzed on the MGI sequencing platform using the Pathogen Fast Identification workflow.

Result

Interestingly the results revealed a low level (0.0266%) of sequencing reads that identified as Naegleria fowleri, a rare amebic pathogen that can cause primary amebic menigioencephalitis (PAM).



PAM caused by Naegleria fowleri infection is extremely rare in China but almost always fatal. The patient went to the Songkran Festival prior to the onset of illness and may have come into contact with sewage. In this case, traditional methods failed to detect the pathogen, however, the MGI high-throughput sequencing platform successfully identified the rare pathogen.



Case 4 Public health issue

Overview

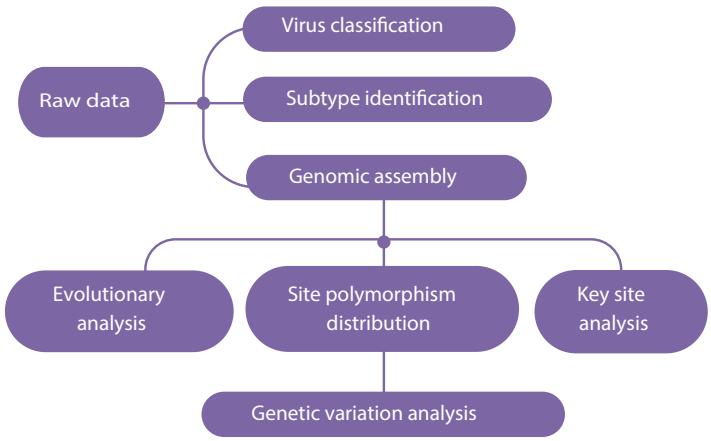
A 45-year-old male returning to China from Angola showed symptoms of Rift Valley fever including fever (38.8 °C), chills, headache, arthralgia, anorexia and enervation on July 13 and was hospitalized for treatment. BGI assisted the Entry-exit Inspection and Quarantine of China to obtain a whole genome sequence of Rift Valley fever virus from the individual using NGS technology. As a result, BGI helped identify, quarantine and treat the individual and prevent a local outbreak of RVF in China.

Solution

RVFV isolation and culture identification were done in biosafety lab of Guangdong Inspection and Quarantine Technology Center. BGI laboratory performed high-throughput sequencing of the sample to gather genomic information about RVFV.

Result

Alignment of the full genome sequence of the RVFV isolate (named RVFV-Beijing strain) revealed 100% identity of three gene segments and 98% homologous to RVFV Kakamas isolate in South Africa.

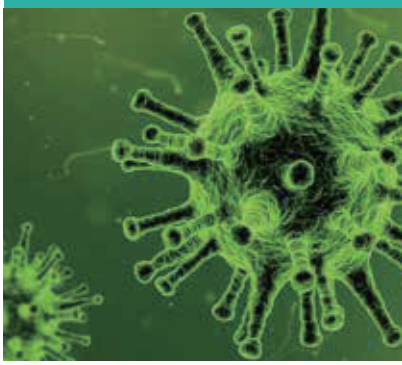


Paper

published on VIROLOGICA SINICA in June 2017


LETTER

Isolation and phylogenetic study of Rift Valley fever virus from the first imported case to China



Case 5 Diagnosis of animal disease

Overview

A group of goats, infected with unknown pathogens developed scabby lesions around their lips, muzzle, and in their mouth. To efficiently control the unknown infection, throat swab samples from the affected goats were tested using MGI Pathogen Fast Identification system（PFI）with a report generated within two days.

Solution

The throat swab samples from goats were processed using the MGI Pathogen Fast Identification system（PFI）with automatic DNA and RNA sample extraction.

Result

A large proportion of sequencing reads in both DNA (64.2%) and RNA (44%) samples mapped directly to the *Orf_virus* which associates closely with the clinical symptoms presented.

Table 5-1 The microorganism identification of DNA and RNA sample from goat swab

Rank	Name of Pathogen	DNA		RNA	
		reads number	relative abundance	reads number	relative abundance
1	*Orf_virus*	358593	64.20%	11311	44%
2	*Pseudocowpox_ virus*	26658	4.80%	650	2.50%
3	*Bacillus_subtilis*	3130	0.60%	518	2.00%
4	*Pseudomonas_aeruginosa*	2011	0.40%	217	0.80%
5	*Staphylococcus_aureus*	1158	0.20%	220	0.90%

Direct comparison of the obtained sequencing reads to reference genome of *Orf_virus* showed 86.7% identity, 87.6% average coverage and 200X depth. (see Figure below)

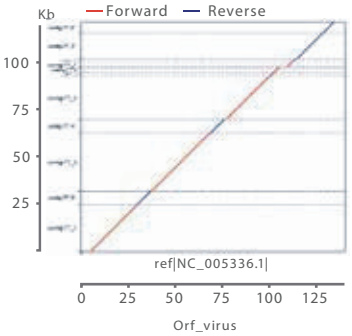


Figure 5-1 Alignment linear graph of assembled sequence and viral genome

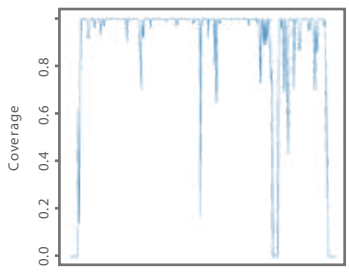


Fig.ure 5-2 Average coverage of viral genome

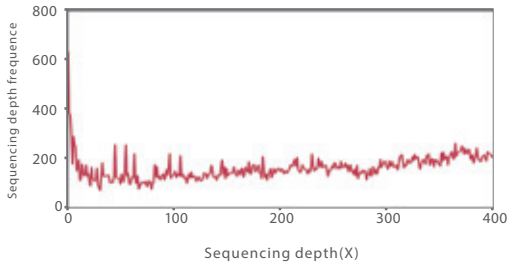


Figure 5-3 Average sequencing depth of viral genome

To verify the result, a traditional PCR assay was then performed and showed positive confirmation of *Orf_virus*. The MGI sequencing technology is a highly accurate method for pathogen identification（PFI）which aids in rapid diagnosis and treatment of animal disease.

Innovate Life Technology

Microbial Detection Total Solution

MGI sequencing platform for pathogen fast identification

MGI Tech Co., Ltd.

▶ Service & Support

MGI has accumulated rich experience in gene sequencing with an excellent team of scientists and engineers, who are committed to providing comprehensive technical support in each section: from the installation, testing and operation, training, maintenance to subsequent upgrades, as well as the laboratory system construction, experiment scheme design and sequencing data analysis. You will experience an unprecedented journey of sequencing.

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*Unless otherwise informed, All sequencers and sequencing reagents are not available in Germany, the US, Spain, the UK, HKSAR and Sweden.

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