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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MGI 华大智造

About us

MGI Tech Co., Ltd. (MGI), a subsidiary of BGI Group, is committed to enabling effective and affordable healthcare solutions for all. Based on its proprietary technology, MGI produces sequencing devices, equipment, consumables, and reagents to support life science research, medicine and healthcare.

MGI's multi-omics platforms include genetic sequencing, mass spectrometry, and medical imaging. Providing real-time, comprehensive, life-long solutions, its mission is to develop and promote advanced life science tools for future healthcare.

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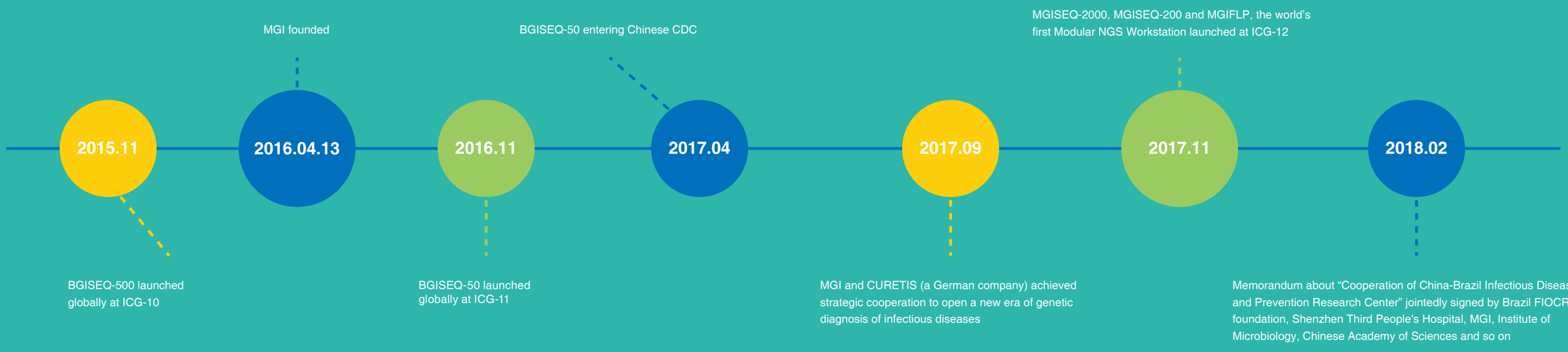
Timeline of MGI Microbial Solutions



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 NGS 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.

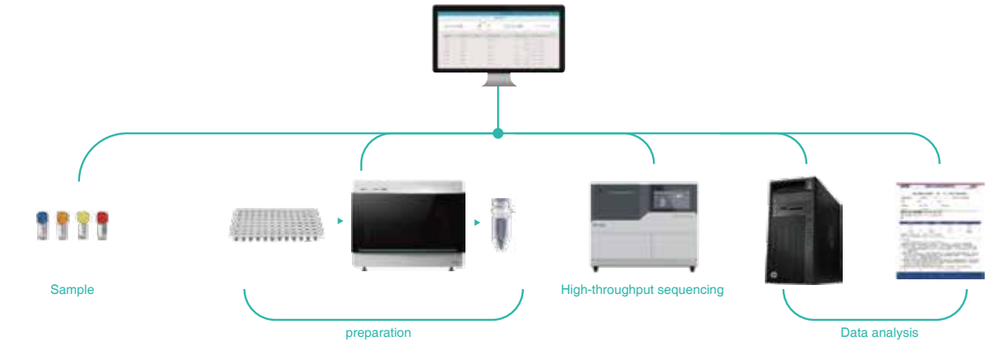
PCR screening

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

Sample
(without culture)



Step 1:Nucleotide extraction | **Step 2:library preparation** | **Step 3:high-throughput sequencing** | **Step 4:data analysis**

Microbial identification report

24 hours from sample to result

Fast, accurate and comprehensive pathogen detection

Applications

MGI NGS platform 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 NGS 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

As a highly-integrated sequencing system, MGI sequencing platform provides quick and reliable data for precise pathogen detection.

Our Advantages

Microbial detection total solution of MGI can perform massive unknown pathogen screening with rapid and precise identification that accurately diagnose and aid treatment decisions. Importantly, our cutting-edge NGS platform benefits routine clinical microbiological diagnosis.

Independent platforms

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

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).

Up-to-date microbial database

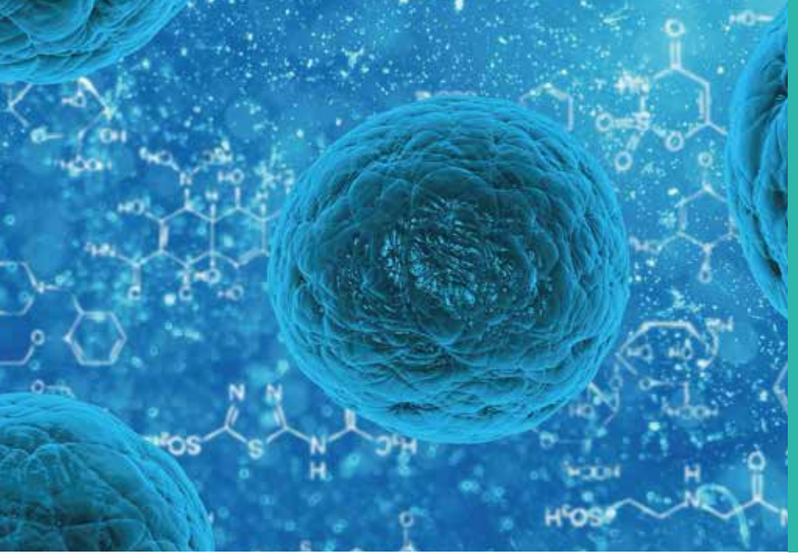
A comprehensive database of 20,000 microbial genomics enabling massive screening at one time.

On-board analysis system

Reliable data analysis at both nucleic acid and protein levels.

Streamlined workflow

24 hours from sample to result-all in one stop.



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 NGS technology to support the real-time diagnosis of infectious diseases.

Genetic Sequencer

Product Information			
Product model	MGISEQ-200	MGISEQ-2000	
Product feature	Efficient	Flexible	
Flow cell	FCS	FCS	FCL
Lane/Chip	1 LANE	2 LANE	4 LANE
Output Model	Medium	Medium	High
Maximum Output/RUN	60 GB	165 GB	1080 GB
Average Effective Signal Point	~ 300 M	~ 550 M	~1800 M
Minimum Read Length	SE50	SE50	
Maximum Read Length	PE100	PE150	
Product Certification	CB,CE, cTUVus and EAC		
Microbial Detection Throughput	up to 16;up to 32;16-96		

Automated sample preparation system

MGISP-100 automated sample preparation system integrates nucleic acid extraction and library preparation into one instrument, providing a fast, stable and highly efficient workflow.

- Nucleic Acid Extraction
- Hybridization Capture and Enzymatic Reactions
- PCR
- Magnetic Bead Purification and Fragment Selection
- Library Pooling
- DNB Preparation

Certification: CE, CB, cTUVus

Independently Developed Analysis Software

Pathogen Fast Identification System

MGI has developed PFI (Pathogen Fast Identification) software with a database containing the genetic information of nearly 20,000 microbes. The integrated system can quickly generate analyses of microbial genome information.

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

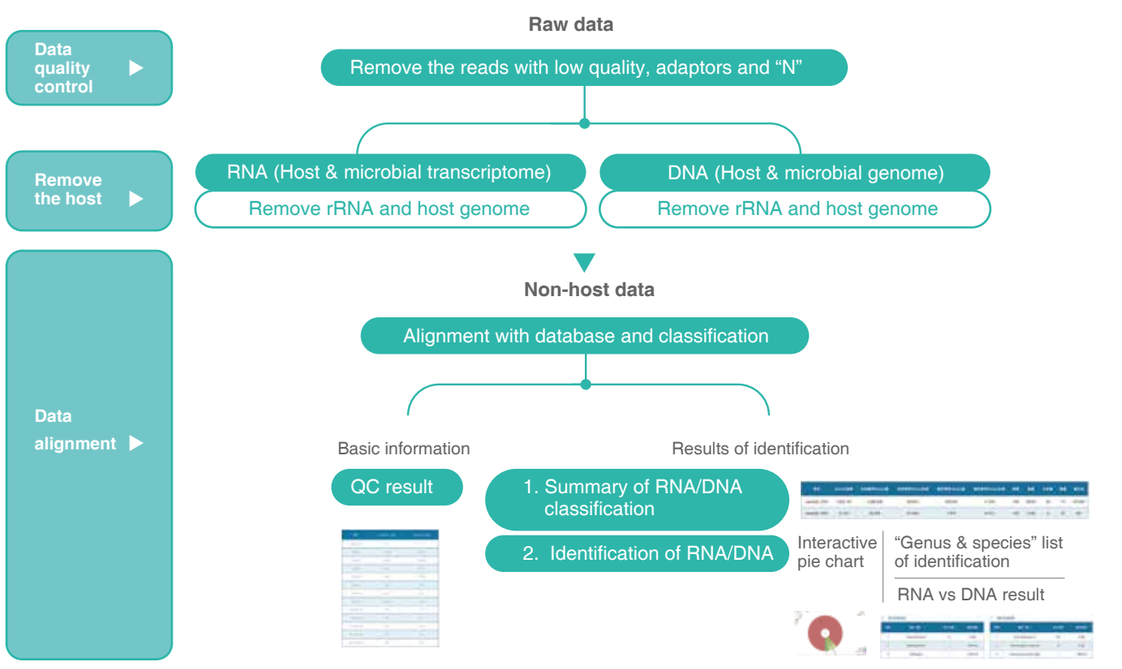
MGI-developed pathogen fast identification system integrates a supported server, database for data analysis, and ZLIMS software for more than data management.

▶ Database

The pathogen fast identification system collects approximately 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	3878	1058
Archaea	470	124
Viruses	7334	729
Fungi	7738	1929
Parasites	551	310

▶ Workflow



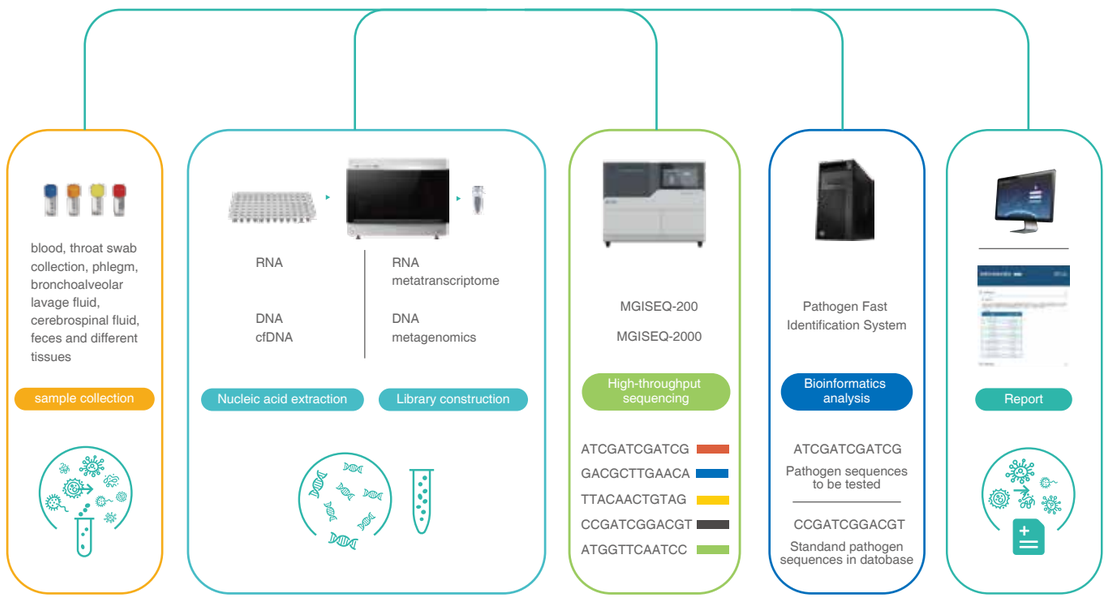
▶ ZLIMS

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

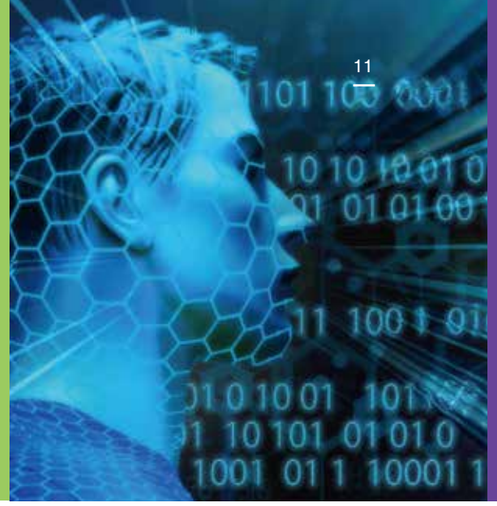
MGI microbial detection total solution **does not require sample culture and preliminary tests**. Additionally, it can identify microorganisms in environmental or clinical samples at one stop.



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

Hands-on operation

Flexible and Comprehensive



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.

▶ Step 1
Nucleic acid extraction

Sample source
Plasma/Blood/ throat swab collection, phlegm, bronchoalveolar lavage fluid, cerebrospinal fluid, feces and different tissues

Extraction kit
MagPure Circulating DNA kitB
MGIEasy Magnetic beads Microbiome DNA extraction Kit
MGIEasy Magnetic beads Viral DNA/RNA extraction Kit

▶ Step 2
Library construction

Nucleic acid source
cfDNA or 150-250bp fragmented DNA
gDNA (mechanical fragmentation)
gDNA (enzymatic fragmentation)
Total RNA

Library construction kit
MGIEasy Cell-free DNA Library Prep Set
MGIEasy Universal DNA Library Prep Set
MGIEasy FS DNA Library Prep Set
MGIEasy RNA Library Prep Set

▶ Step 3
High-throughput sequencing

MGISEQ-2000 MGISEQ-200

High-throughput sequencing
MGISEQ-2000RS High-throughput Sequencing Set
MGISEQ-200RS High-throughput Sequencing Set

▶ Step 4
Bioinformatics analysis

Analysis server of bioinformatics

Analysis software
Pathogen Fast Identification System

Hands on time Automatic time

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

Sample source
Plasma/Blood/ throat swab collection, phlegm, bronchoalveolar lavage fluid, cerebrospinal fluid, feces and different tissues

Extraction kit
MagPure Circulating DNA kitB
MGIEasy Magnetic beads Microbiome DNA extraction Kit
MGIEasy Magnetic beads Viral DNA/RNA extraction Kit

▶ Step 2
Library construction

Nucleic acid source
cfDNA or 150-250bp fragmented DNA
gDNA (enzymatic fragmentation)
Total RNA

Library construction kit
MGIEasy Cell-free DNA Library Prep Set
MGIEasy FS DNA Library Prep Set
MGIEasy RNA Library Prep Set

MGISP-100

▶ Step 3
High-throughput sequencing

MGISEQ-2000 MGISEQ-200

High-throughput sequencing
MGISEQ-2000RS High-throughput Sequencing Set
MGISEQ-200RS High-throughput Sequencing Set

▶ Step 4
Bioinformatics analysis

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 generates 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 identification
2.3 RNA identification	2.4 RNA vs DNA

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 Identification of a novel or variant pathogen strain

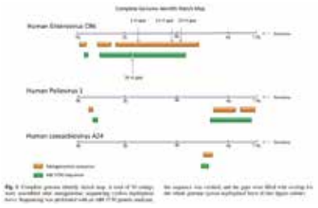
Overview

A 4-year-old boy was hospitalized with clinical presentations of hand-foot-and-mouth disease including fever and vesicular exanthema on his hands, feet, oral mucosa, and anus for 1 week. The qRT-PCR results revealed that the causative agent was HEV instead of EV71 or CVA16. To further verify the pathogen, a stool sample was collected from the patient for metagenomic sequencing.

Analysis server of bioinformatics

Solution

The stool specimen was collected for Pathogen Fast Identification with automated RNA isolation, library preparation and high-throughput sequencing.

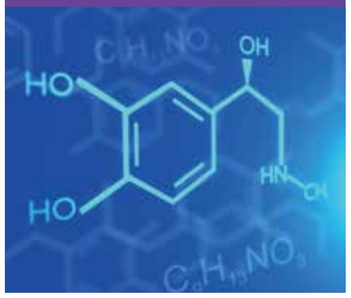


Result

Ten non-overlapping contigs were assembled after high-throughput sequencing and verified by mapping to the genomes of three pathogens: human coxsackievirusA24, enterovirus96, and human poliovirus 1. Primers were used to amplify the sequences and analysis suggested that all the contigs belonged to a consensus sequence of new strain EV-96. It is the first time that metagenomic sequencing has been used to identify an EV-96 strain as the cause of HFMD.

Paper

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



Case 2 Identification of co-infections

Overview

A 26-year-old woman developed a mild respiratory illness on Jan. 28, 2017, but symptoms progressed to recurrent fever, cough, chills, expectoration, slight hemoptysis, muscle and joint pain in the following days. On February 3, the patient was hospitalized due to worsening symptoms of cyanotic lips, fever of 39.3 °C, heart rate of 144 beats/ min and diagnosed with severe pneumonia with ARDS. She was treated with antibiotics and antiviral therapies and then discharged on February 17. Blood and respiratory secretions were collected during her hospitalization for pathogen testing. The screening results from bacteria and fungi culture-based test, G-test and GM-test were all negative. In addition, HIV, HBV, influenza viruses, SARS-CoV, MERS- CoV and other coronaviruses were negative by ELISA and/or (RT-)PCR assays.

Solution

Pulmonary secretions from the patient were collected on the first day of hospitalization and analyzed using metagenomic sequencing to determine the cause of infection.

Analysis server of bioinformatics

Result

Two respiratory viruses, HRV and HBoV were identified in high abundance using sequencing and confirmed by specific (RT-)qPCR assays and a report generated to diagnose acute co-infection of HBoV1 and HRV-C.

In this case, metagenomic sequencing showed a significant advantage in detection of the causative agents of severe illness over traditional methods such as culture, ELISA, PCR, etc. because prior knowledge was not assumed or required.

Total=2166 Figure B Viral reads distribution.

Paper

Metagenomic analysis identified co-infection with human rhinovirus C and bocavirus 1 in an adult suffering from severe pneumonia Published on Journal of Infection in March 2018

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-presentation, 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.

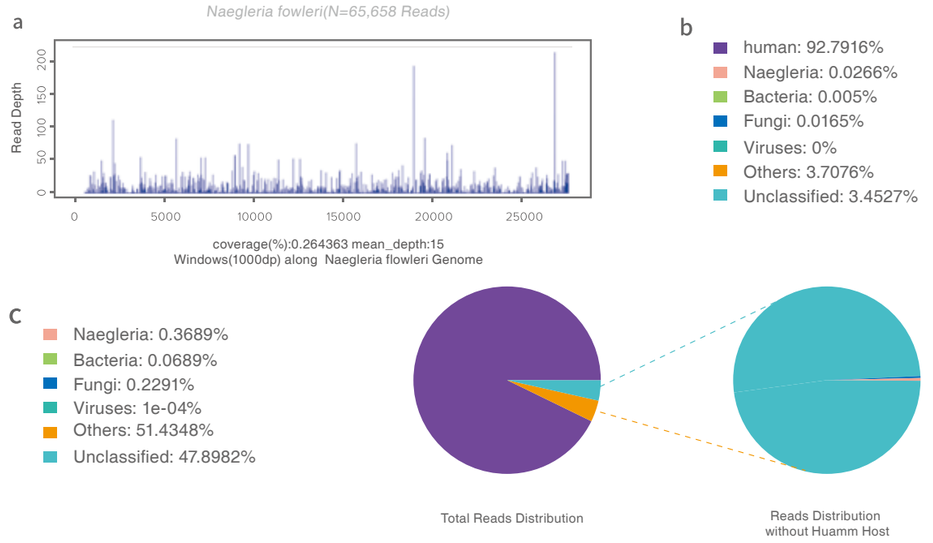
Solution

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

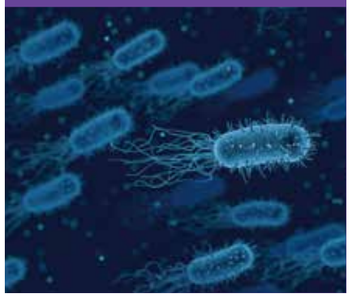
Analysis server of bioinformatics

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.

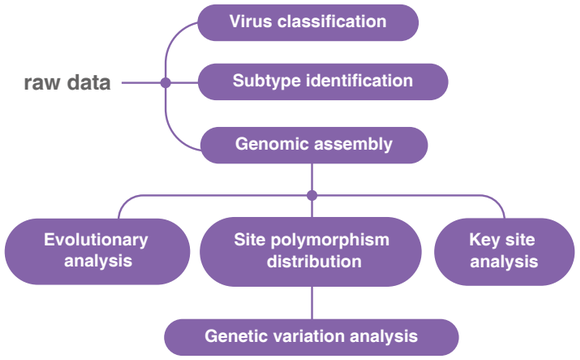
Solution

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.

Analysis server of bioinformatics

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 with a report generated within two days.

Solution

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

Analysis server of bioinformatics

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 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 genome showed 86.7% identity, 87.6% average coverage and 200X depth. (see Figure below)

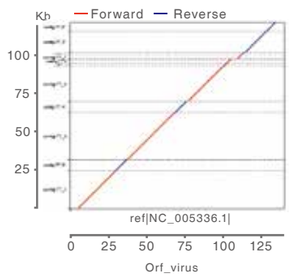


Fig.1 Alignment linear graph of assembled sequence and viral genome

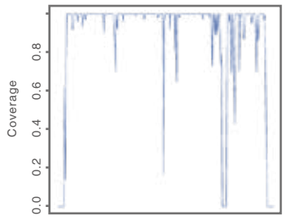


Fig.2 Average coverage of viral genome

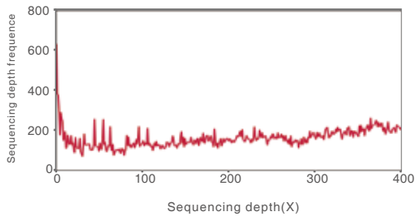


Fig.3 Average sequencing depth of viral genome

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 which aids in rapid diagnosis and treatment of animal disease.