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 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.

**Timeline of MGI Microbial Solutions**

- **2015.11**: MGI founded
- **2016.04.13**: BGISEQ-50 entering Chinese CDC
- **2016.11**: BGISEQ-500 launched globally at ICG-10
- **2017.04**: BGISEQ-50 launched globally at ICG-11
- **2017.09**: BGISEQ-2000, MGISEQ-200 and MGIFLP, the world’s first Modular NGS Workstation launched at ICG-12
- **2017.11**: MGI and CURETIS (a German company) achieved strategic cooperation to open a new era of genetic diagnosis of infectious diseases
- **2018.02**: Memorandum about “Cooperation of China-Brazil Infectious Diseases and Prevention Research Center” jointly signed by Brazil FIOCRUZ foundation, Shenzhen Third People’s Hospital, MGI, Institute of Microbiology, Chinese Academy of Sciences and so on
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 various hardware devices and compatible reagent kits for the system to support an extensive range of pathogen testing.

Traditional pathogen detection methods

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOF-MS (Time-of-flight mass spectrometry)</td>
<td>Need clonal isolates.</td>
</tr>
<tr>
<td>Immunoassay</td>
<td>Sensitivity and specificity issues.</td>
</tr>
<tr>
<td>PCR screening</td>
<td>Can only detect known pathogens and prone to assay specific limitations.</td>
</tr>
</tbody>
</table>

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
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:

### Applications

<table>
<thead>
<tr>
<th>Animal health</th>
<th>Agriculture</th>
<th>Travel health</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Animal health" /></td>
<td><img src="image2.png" alt="Agriculture" /></td>
<td><img src="image3.png" alt="Travel health" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Animal science and medicine</th>
<th>Public health</th>
<th>Prevention and control of human and animal diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image4.png" alt="Animal science and medicine" /></td>
<td><img src="image5.png" alt="Public health" /></td>
<td><img src="image6.png" alt="Prevention and control of human and animal diseases" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Food safety</th>
<th>Public healthcare</th>
<th>Precision medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image7.png" alt="Food safety" /></td>
<td><img src="image8.png" alt="Public healthcare" /></td>
<td><img src="image9.png" alt="Precision medicine" /></td>
</tr>
</tbody>
</table>

### Our Advantages

- **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 20,000 microbial genomics enabling massive screening at one time.

- **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.

- **Streamlined workflow**
  24 hours from sample to result—all in one stop.

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.

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.
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.

MGI’s fully-integrated sequencing system enables NGS technology to support the real-time diagnosis of infectious diseases.

**Independently developed platforms**

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.

**Genetic Sequencer**

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

**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.

**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.
Our Solution

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.

<table>
<thead>
<tr>
<th>Microbial classification</th>
<th>Species</th>
<th>Genus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteria</td>
<td>3878</td>
<td>1058</td>
</tr>
<tr>
<td>Archaea</td>
<td>470</td>
<td>124</td>
</tr>
<tr>
<td>Viruses</td>
<td>7334</td>
<td>729</td>
</tr>
<tr>
<td>Fungi</td>
<td>7738</td>
<td>1929</td>
</tr>
<tr>
<td>Parasites</td>
<td>551</td>
<td>310</td>
</tr>
</tbody>
</table>

Workflow

Raw data
- Remove the reads with low quality, adaptors and "N"
- RNA (Host & microbial transcriptome)
- DNA (Host & microbial genome)

Non-host data
- Remove rRNA and host genome
- "Genus & species" list of identification

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

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

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.
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.
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.

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

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.

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

Ten non-overlapping contigs were assembled after high-throughput sequencing and verified by mapping to the genomes of three pathogens: human coxsackievirus A24, enterovirus 96, 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.

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

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.

### 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.

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

### Solution

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.

### Result

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.

### Paper

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**

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 Kakamaa isolate in South Africa.

**Paper**
published on Virologica Sinica in June 2017

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**Case 5 Diagnosis of animal disease**

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.

**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**

<table>
<thead>
<tr>
<th>Rank</th>
<th>name of pathogen</th>
<th>DNA reads number</th>
<th>DNA relative abundance</th>
<th>RNA reads number</th>
<th>RNA relative abundance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Orf_virus</td>
<td>358593</td>
<td>64.20%</td>
<td>11311</td>
<td>44%</td>
</tr>
<tr>
<td>2</td>
<td>Pseudocowpox_virus</td>
<td>26658</td>
<td>4.80%</td>
<td>650</td>
<td>2.50%</td>
</tr>
<tr>
<td>3</td>
<td>Bacillus_subtilis</td>
<td>3130</td>
<td>0.60%</td>
<td>518</td>
<td>2.00%</td>
</tr>
<tr>
<td>4</td>
<td>Pseudomonas_aeruginosa</td>
<td>2011</td>
<td>0.40%</td>
<td>217</td>
<td>0.80%</td>
</tr>
<tr>
<td>5</td>
<td>Staphylococcus_aureus</td>
<td>1158</td>
<td>0.20%</td>
<td>220</td>
<td>0.90%</td>
</tr>
</tbody>
</table>

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)

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.