CapitalBio Corporation

博奥晶典 CapitalBio Technology

# CapitalBio Rapid Genetic Detection of TB/NTM Infections and Drug Resistance

## Product Specifications and Clinical Applications

**Tuberculosis (TB)** – is a top infectious disease killer worldwide. In 2014, 9.6 million people fell ill with TB and 1.5 million died from the disease.

## Multidrug– Resistant TB (MDR–TB) is Widespread in the World

Multidrug–resistant TB (MDR–TB) is caused by TB bacteria that are resistant to at least isoniazid and rifampicin, the two most effective TB drugs. Based on figures from 2014, the latest year for which data are available, WHO estimates that 5% of TB cases are multidrug–resistant. This translates into 480,000 cases and 190,000 deaths each year.

## Extensively Drug–Resistant TB (XDR–TB)

Extensively drug–resistant TB (XDR–TB) is a form of MDR–TB that is also resistant to any fluoroquinolone and any of the second – line anti–TB injectable agents (i.e. amikacin, kanamycin or capreomycin). About 9% of MDR–TB patients develop XDR–TB, which is even more difficult to treat.

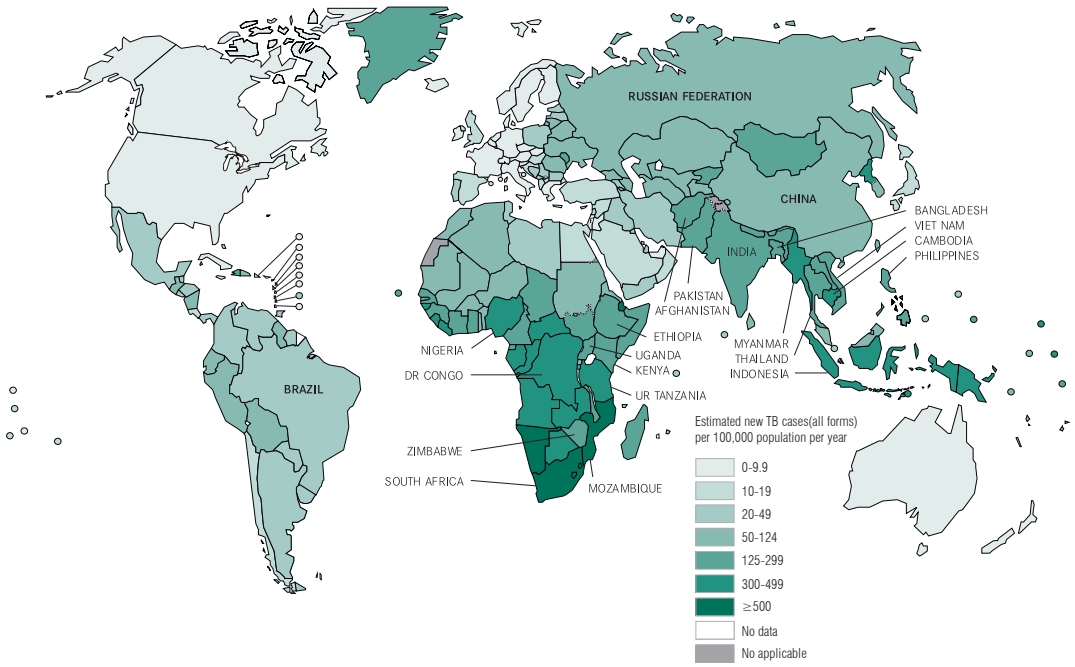
## Increasing HIV Coinfection in TB Patients

TB is a leading killer of HIV–positive people: in 2015, 1 in 3 HIV deaths was due to TB.

## Importance of Rapid Diagnostics on TB Drug Resistance

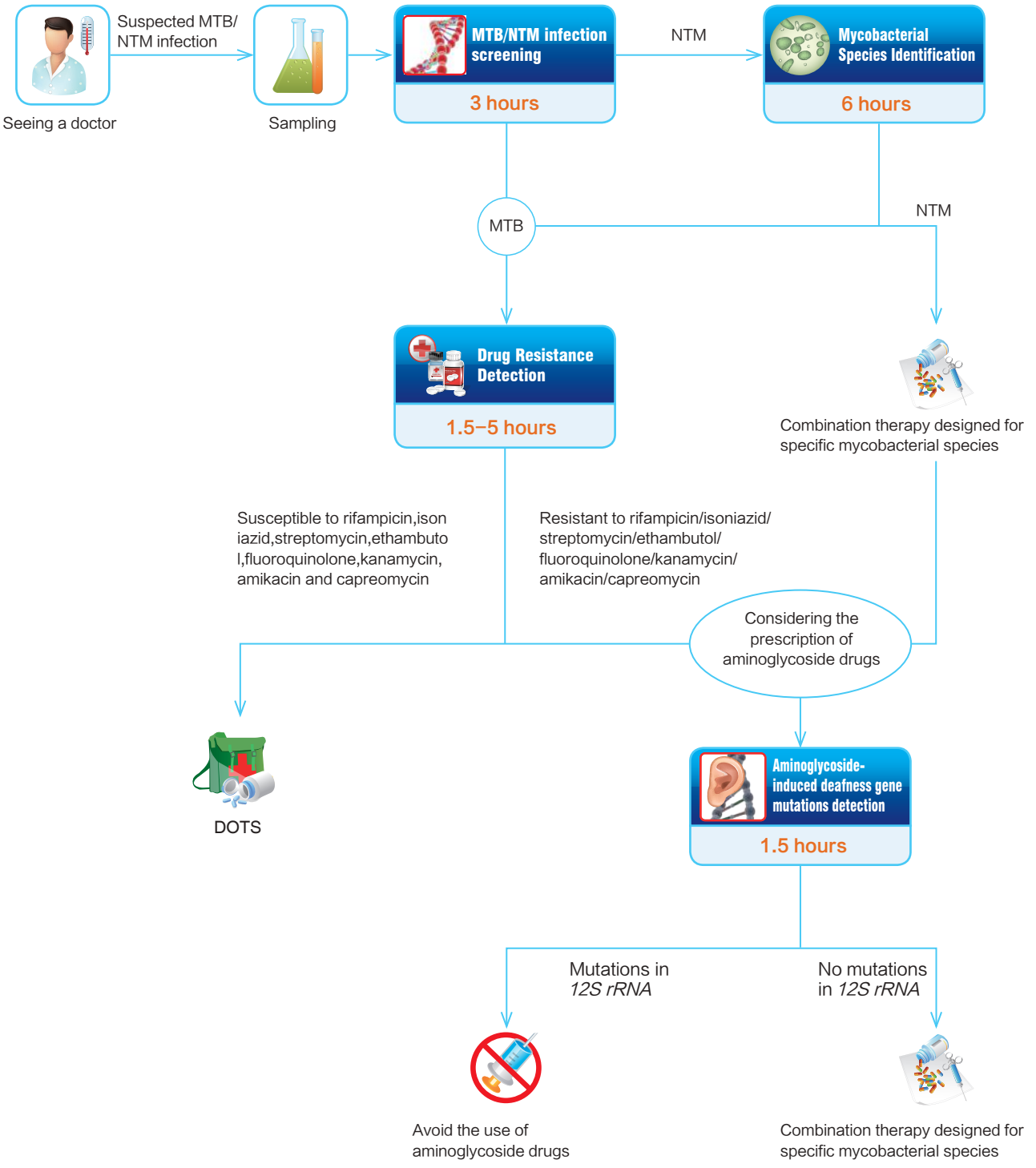
Rapid diagnostics of multidrug–resistance TB (MDR–TB) and extensively drug–resistant TB (XDR–TB) would facilitate early administration of appropriate therapies and is crucial to reduce the spread of drug resistant strains, while conventional drug susceptibility testing (DST) of M. tuberculosis specimens is time–consuming, taking several weeks or even longer to complete.

### Estimated TB incidence rates, 2014




Data sourced from WHO

# Total Solution for TB Screening & Monitoring Strategy



# CapitalBio Tuberculosis and Non-tuberculous Mycobacteria Real-time PCR Detection Kit

*——Rapid and Accurate TB Screening Product*

Detection Time
Less Than 3 Hours

## Description

The Kit can rapidly detect *M. tuberculosis* and/or non-tuberculous mycobacteria infections thus is important to decide the proper remedy as early as possible.

CapitalBio Tuberculosis and Non-tuberculous Mycobacteria Real-time PCR Detection Kit utilizes real time fluorescence PCR technology and TaqMan probe technology. Specific primers and probes are designed for *M. tuberculosis* and non-tuberculous mycobacteria respectively. The two probes are labeled with different fluorescences, thus can be used to detect *M. tuberculosis* and / or non-tuberculous mycobacteria in the same single tube.

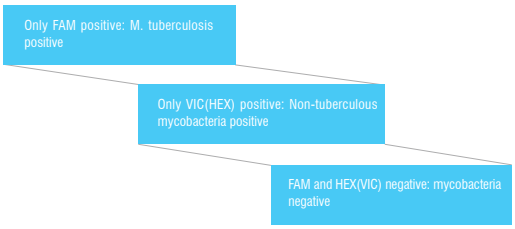
## Key Features

- **Accurate:** The real time fluorescence quantitative PCR method is used to compare the results in a real time manner and effectively eliminate random errors. The specificity is 99% and the sensitivity for culture-positive samples is 97% for 1,025 cases in clinical trials
- **Rapid:** The whole detection process is less than 3 hours
- **Efficient:** The infections of *M. tuberculosis* and / or non-tuberculosis mycobacteria can be rapidly detected simultaneously in one tube, one test
- **Sensitive:** Specific primers and probes are designed for *M. tuberculosis* and non-tuberculous mycobacteria respectively. The detection limit is as low as 10 bacteria / PCR reaction (for *M. tuberculosis*) and 100 bacteria / PCR reaction (for non-tuberculous mycobacteria)
- **Advanced:** Based on the TaqMan probe technology and the real time fluorescence PCR technology

## Workflow

DNA Extraction

Real time fluorescence quantitative PCR Cycler




## Certifications

CE IVD

# CapitalBio Mycobacteria Identification Array Kit

*————A Powerful Tool for the Early Diagnosis of NTM Infections*

## Description

Detection Time
Less Than 6 Hours

Non-tuberculosis mycobacteria (NTM) have been recognized as an important cause of disease in immuno-compromised hosts such as AIDS patients. Most of the NTM infections are naturally resistant to many common antibiotics. The ability to identify Mycobacterium tuberculosis complex (MTC) isolates and differentiate them from NTM is therefore important for patient management, the choice of antimicrobial therapy, hospital control of infection, and for public health TB control services.

The DNA extracted from clinical isolates or specimens is used as a template for PCR. The PCR primers are fluorescently tagged, resulting in fluorescently tagged amplified PCR products. The PCR products are then hybridized to a microarray slide spotted with species test sequences, using the optimized hybridization buffer. After washing and drying, the chips are imaged using a microarray scanner. The kit interpretation software then analyzes the scanned data to generate the test reports, based on the distribution of positive fluorescent probe signals on the microarray.

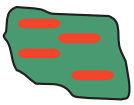
CapitalBio Mycobacteria Identification Array Kit provides a novel method to identify 17 mycobacterial species that are most frequently isolated in clinical laboratories, including:

- *M. tuberculosis complex*
- *M. intracellulare*
- *M. avium*
- *M. gordonae*
- *M. kansassi*
- *M. fortuitum*
- *M. scrofulaceum*
- *M. gilvum*
- *M. terrae*
- *M. chelonae*
- *M. abscessus*
- *M. phlei*
- *M. nonchromogenicum*
- *M. marinum*
- *M. ulcerans*
- *M. aurum*
- *M. szulgai*
- *M. xenopi*
- *M. smegmatis*

## Key Features

- **Simple and Safe:** DNA extraction can be performed either from isolated strain cultures or directly from clinical sputum samples
- **Fast analysis:** The entire detection time required is less than 6 hours. This is remarkably shorter than traditional biochemical methods which require at least four weeks
- **High sensitivity:** Higher sensitivity than other competitive methods, due to specially designed primer pairs and multiplex PCR procedures
- **High throughput:** Tuberculosis pathogens and 16 non-tuberculous mycobacteria from patient specimens
- **High consistency:** Strict step-by-step quality controls are used throughout the whole process, plus automatic data analysis assuring precise and reproducible results
- **Excellent reliability:** The specific system prevents PCR-contamination
- **Total solution:** The system includes all the reagents, instruments and analysis software

# Workflow



Sputum

DNA Extraction

Gene Amplification

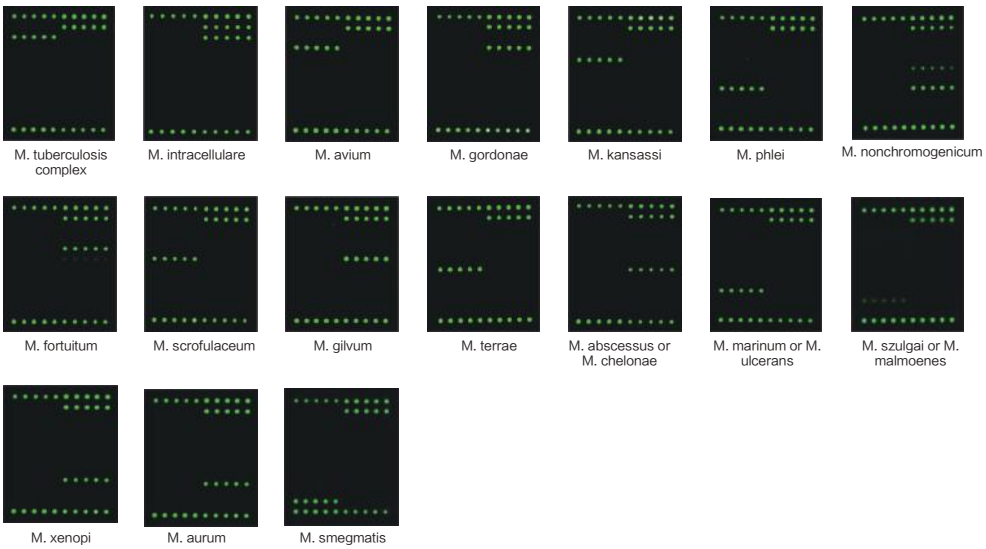
Array Clean-up

Array Hybridization

Array Scanning

Data Analysis

# Images of Positive Results




# Clinical Performance

| Hospital | Samples | | | Total |
|---|---|---|---|---|
| | MTB | NTM | Control | |
| Beijing CH | 577 | 201 | 53 | 831 |
| Shanghai CH | 383 | 117 | 53 | 553 |
| Guangzhou CH | 138 | 149 | 53 | 340 |
| Total | 1,098 | 467 | 159 | 1,724 |
| | 1,565 | | | |

# Certifications

CE IVD

# CapitalBio *M.Tuberculosis* Drug Resistance Gene Real-Time PCR Detection Kit

*——Powerful Assistant to Multi Drug Resistant TB (MDR) Rapid Diagnosis*

## Description


CapitalBio *M. tuberculosis* Drug Resistance Gene Real-Time Detection Kit is intended for the detection of some frequently observed site mutations in seven genes which strongly implicate resistance to eight important first-line and second-line anti-tuberculosis drugs ( rifampicin, isoniazid, streptomycin, ethambutol, fluoroquinolone , kanamycin, amikacin and capreomycin ). Genomic DNA is extracted for testing directly from a clinical isolate culture or pulmonary smear-positive clinical specimens. The whole detection assay takes only 1.5 hours, which is notably shorter than susceptibility tests that require at least 4 weeks or longer time. *M. tuberculosis* Drug Resistance Gene Real-Time Detection Kit has the combination of specific primer and probe designs, strictly controlled PCR procedure, real-time PCR process and automatic software analysis providing rapid personalized therapy advice.

The *M. tuberculosis*-specific primers and the TaqMan MGB probes are designed based on the mutations of the *rpo*B gene, *kat*G gene and regulatory region of *inh*A gene, *emb*B gene, *gyr*A gene, *rps*L gene and *rrs* gene. As TaqMan minor groove binder probes can distinguish one-base mismatches, the real-time PCR system in combination with MGB probes has been applied to analyze single-nucleotide polymorphism. Thus, the specific TaqMan MGB probes can recognize different mutations.

## Key Features

- **More detection indexes:** Rapidly detect drug resistance to 8 most important first-line and second-line drugs
- **Fast analysis:** The entire detection time takes only 1.5 hours, this is remarkably shorter than traditional biochemical methods which require at least 4 weeks or longer time
- **Simple and Safe:** DNA extraction can be performed either from isolated strain cultures or directly from clinical sputum samples
- **High sensitivity:** Higher sensitivity than other competitive methods, due to specially designed primer pairs and multiplex PCR procedures
- **High throughput:** 20 mutations of 7 genes (*rpo*B, *kat*G, *inh*A, *rps*L, *emb*B, *gyr*A and *rrs*) can be detected simultaneously
- **High consistency:** Strict step-by-step quality controls are used throughout the whole process, plus automatic data analysis assuring precise and reproducible results
- **Excellent reliability:** The specific system prevents PCR-contamination

# Workflow

DNA Extraction

Real time fluorescence quantitative PCR Cycler

# Clinical Performance

| Clinical Testing Results of CapitalBio *M.Tuberculosis* Drug Resistance Gene Real-Time PCR Detection Kit | | | | |
|---|---|---|---|---|
| No. | Drug Resistance Testing Results | Total Tested Clinical Specimens | Coincidence Rate of Clinical Specificity | Clinical Sensitivity |
| 1 | Rifampicin | 1200 | 97.92% | 1000 Bacteria /mL |
| 2 | Isoniazid | 1200 | 98.08% | |
| 3 | Ethambutol | 1200 | 97.94% | |
| 4 | Fluoroquinolone | 1200 | 97.68% | |
| 5 | Streptomycin | 1200 | 97.39% | |
| 6 | Kanamycin/Amikacin/Capreomycin | 1200 | 98.31% | |

# Certifications

CE IVD

# CapitalBio *M.tuberculosis* Drug Resistance Detection Array Kit

*——Powerful Assistant to Multi Drug Resistant TB (MDR) Rapid Diagnosis*

## Description

Detection Time
5 Hours

The Mycobacterium tuberculosis drug resistance array is designed to detect the most frequently observed drug resistances of Mycobacterium tuberculosis (MTB), to Rifampicin and Isoniazid. The MTB-specific primers and the corresponding oligonucleotide probes are designed based on the mutations of the *rpo*B gene (conferring resistance to rifampicin), *kat*G gene and promoter of *inh*A gene (conferring resistance to Isoniazid).

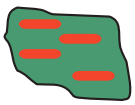
CapitalBio *M.tuberculosis* Drug Resistance Detection Array Kit is based on pathogen nucleic acid test with DNA microarray, which can investigate multi drug resistance (to rifampin and isoniazid) of *M. tuberculosis* by site mutation detection of *rpo*B / *kat*G / *inh*A.

| Drugs | Rifampin | Isoniazid | |
|---|---|---|---|
| Related Genes | *rpo*B Gene | *Kat*G Gene | *inh*A Gene |
| Hot Spots | 511, 513, 516, 526, 531, 533 | 315 | −15 |

## Key Features

- **Accurate:** The software generates reports automatically and eliminates human errors; Special design to avoid contamination during PCR; 100% consistent with sequencing for 1,186 cases in clinical trials
- **Rapid:** Reduce the detection time from 4 ~ 8 weeks for conventional methods to 6 hours
- **Efficient:** The drug resistances to rifampin and isoniazid are detected at the same time
- **Sensitive:** 1 × $10^3$ bacteria / reaction
- **Advanced:** Based on our proprietary DNA microarray technology

## Workflow



Sputum Sample

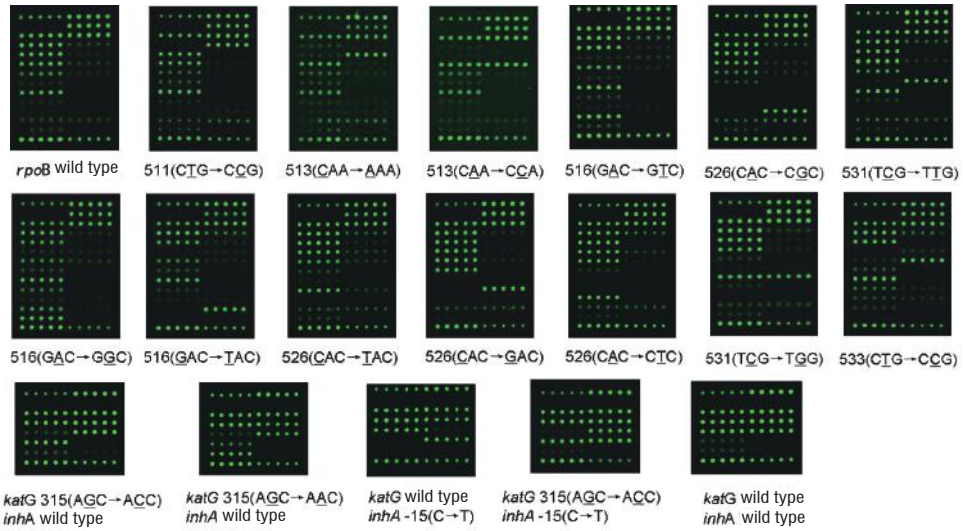
Bacteria DNA Extraction

PCR Amplification

Microarray Scanning and Result Interpretation

Hybridization Reaction

# Images of Positive Results




# Clinical Performance

| Hospital | Drug Sensitive Cases | Drug Resistant Cases | Total |
|---|---|---|---|
| Beijing Chest Hospital | 149 | 425 | 574 |
| Shanghai Chest Hospital | 155 | 320 | 475 |
| Guangzhou Chest Hospital | 76 | 61 | 137 |
| Total | 380 | 806 | 1,186 |

## Rifampin

| Genotype | RFP DST | | | Sensitivity | Specificity | Con |
|---|---|---|---|---|---|---|
| | R | S | Total | | | |
| Mutant | 736 | 11 | 747 | 92.0% | 97.2% | 93.7% |
| Wild | 64 | 375 | 439 | | | |
| Total | 800 | 386 | 1,186 | | | |

Consistency with sequencing: 100%

## Isoniazid

| Genotype | INH DST | | | Sensitivity | Specificity | Con |
|---|---|---|---|---|---|---|
| | R | S | Total | | | |
| Mutant | 617 | 12 | 629 | 77.4% | 96.9% | 83.8% |
| Wild | 180 | 377 | 557 | | | |
| Total | 797 | 389 | 1,186 | | | |

Consistency with sequencing: 100%

# Certifications

CE IVD

# CapitalBio Aminoglycoside-Induced Deafness Gene Mutations Detection Kit

## Description

Exposure to aminoglycoside antibiotics such as streptomycin can lead to severe-to-profound hearing loss. A single base-pair substitution from an A to a G at position 1555 in *12S rRNA* gene predisposes individuals to aminoglycoside ototoxicity. Evidence has shown that even a single dose of an aminoglycoside antibiotic results in irreversible hearing loss in individuals with this mutation. A recent report showed that the homoplasmic *12S rRNA* C1494T mutation was also associated with hearing loss. Aminoglycoside antibiotics are important anti-tuberculosis drugs. It should be mandatory to detect these mutations when aminoglycoside antibiotics must be used.

Aminoglycoside-Induced Deafness Gene Mutations Detection Kit is designed for a rapid and accurate detection of gene mutations related to deafness caused by the use of aminoglycosides. It employs fluorescence quantitative PCR technology and covers two mutations in one gene. It helps to identify individuals likely to suffer hearing loss after using aminoglycosides and allows precautions to be taken to avoid deafness caused by inappropriate use of aminoglycosides.

| Gene | Locus | Mutation |
|---|---|---|
| *12S rRNA* | 1494 | 1494 C>T |
| | 1555 | 1555 A>G |

## Key Features

- **High accuracy and efficiency:** Rapid and accurate detection of gene mutations related to deafness caused by the use of aminoglycosides
- **Fast analysis:** The entire detection time is 1.5 hours
- **High sensitivity:** Its detection limit is 3ng human genomic DNA/ μ L
- **High consistency:** Strict step-by-step quality controls are used throughout the whole process, plus automatic data analysis assuring precise and reproducible results
- **Excellent reliability:** The specific system prevents PCR-contamination

## Workflow

DNA Extraction

Real time fluorescence quantitative PCR Cycler

## Clinical Performance

100% consistency with SBT

201606

CapitalBio Corporation | 博奥晶典 CapitalBio Technology


CapitalBioTech: Building C, Block 88 Kechuang 6th Street
Yizhuang Biomedical Park
Beijing Economic-Technological Development Area
Beijing 101111
China
Tel: +86-10-69002900 Ext. 8801
Fax: +86-10-69002988
Email: globalsales@capitalbiotech.com

USA: 10225 Barnes Canyon Rd., Ste. A 108
San Diego, CA 92121
USA
Tel: 1-858 202 1791
Fax: 1-858 202 1795
Email: globalsales@capitalbiotech.com


***Website: https://www.capitalbiotechnology.com/***