

# TB tNGS

## GeneMind NGS-based Solutions for Tuberculosis(TB) Genetic Detection and Drug-resistance Analysis

### Accurate data performance

- Accurate characterization of nucleotide-level genetic polymorphisms
- Detailed sequence information for multiple gene regions or whole genomes

### Wide range of annotation

- Detection of resistance to a wide range of first and second-line anti-tuberculosis drugs
- Detection of mixed infection and heteroresistance down to 3% of subpopulations

### Automated workflow

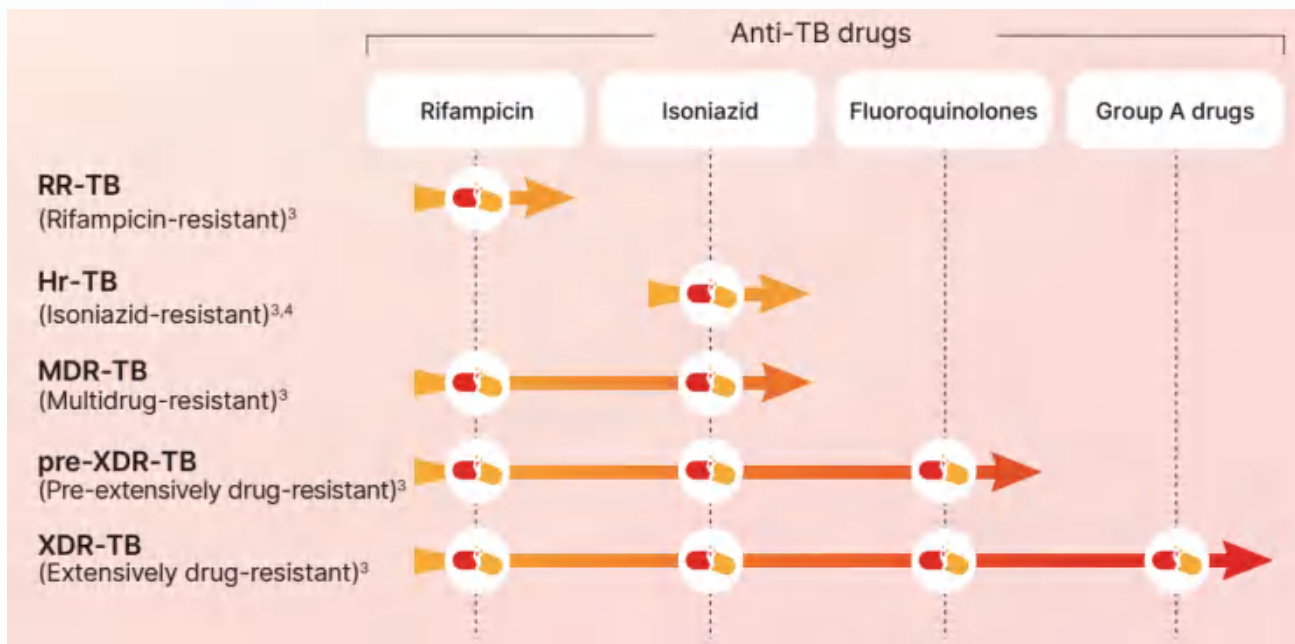
- Automated and simplified sequencing and data analysis workflow
- Quick test from sample preparation to final report within 42 hours



## ◆ Background

TB is an infectious disease caused by bacteria in the Mycobacterium tuberculosis complex (MTBC), which includes *M. tuberculosis* (Mtb). Mtb typically infects the lungs and is spread when infected persons expel bacteria into the air. TB continues to have a huge annual global impact with 6.4 million newly diagnosed cases and 1.6 million TB-associated deaths in 2021.

Drug-resistant TB (DR-TB) refers to a TB infection that is resistant to one or more anti-TB drugs. The ability of TB to resist anti-TB drugs represents a major barrier to TB diagnostic, treatment, and eradication efforts. Since Mtb is continually adapting to new anti-TB drugs and evolving cognate resistance mutations, there is a need for a faster and more accurate method to distinguish drug-resistance properties. NGS is fueling the future of the DR-TB research landscape. GeneMind tNGS workflows can be applied to TB genomic investigation, providing crucial and precise TB detection and drug resistance profiling. This information is critical and helpful for doctors to make best decisions on multiple and extensively drug-resistant tuberculosis (M/XDR-TB) treatment plan in time.

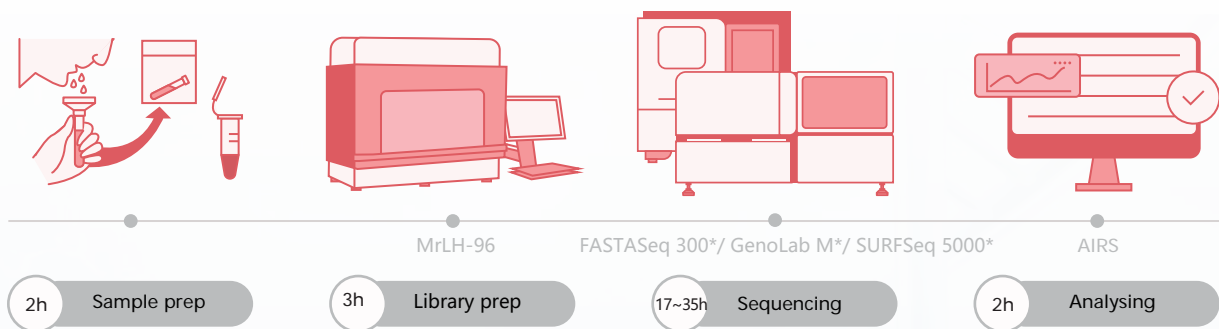


## ◆ Product Introduction

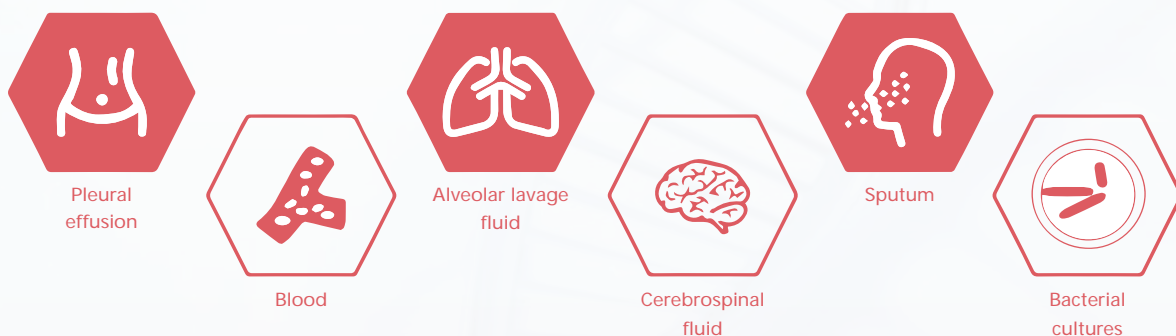
Based on tNGS technology and GeneMind high throughput sequencing platforms (GenoLab M\*, FASTASeq 300\* and SURFSeq 5000\*), GeneMind has launched a fully automated end-to-end solution of TB drug resistance detection products. This solution can directly sequence sputum and other samples of patients quickly and accurately, without cell culture process. It helps to speed up the early detection of infectious sources, diagnosis of tuberculosis, clear TB drug resistance situation and provide the guideline for clinical treatment.

Parameter	TB-tNGS		
Sample type	Sputum, Alveolar lavage fluid, Pleural effusion, Blood, Cerebrospinal fluid, Bacterial cultures		
Sample volume	≥0.5 mL		
Library preparation	multiplex PCR		
Method	Targeted sequencing		
Sequencing platform	GenoLab M*	FASTASeq 300*	SURFSeq 5000*
No. of samples/run	1 FCM: 96 1 FCH/2 FCM: 192 1 FCM+1 FCH: 288 2 FCH: 384	1 FCM: 36 1 FCH: 96	1 FCM: 192 1 FCH: 768 1 FCM+1 FCH: 960 2 FCM: 384 2 FCH: 1536
Turnaround time	42h	24h	41h
Sequencing strategy	PE100, ≥2 M raw reads per sample		
Report generation	Local analysis and report system		

## ◆ Automated Workflow



## ◆ Sample Type



## ◆ Drug-resistance Gene List

Drug-Resistance Gene List		
	Drug Type	Gene List
First-line anti-tuberculosis drugs (4)	Rifampicin	<i>rpoB</i>
	Isoniazid	<i>fabG1, katG</i>
	Ethambutol	<i>embB</i>
	Pyrazinamide	<i>pncA</i>
Second-line anti-tuberculosis drugs (8)	Streptomycin	<i>rpsL, gid</i>
	Ethionamide	<i>ethA, fabG1, inhA</i>
	Para-aminosalicylic acid	<i>folC, ribD, thyA</i>
	Levofloxacin	<i>gyrA, gyrB</i>
	Cycloserine	<i>alr</i>
	Kanamycin	<i>eis</i>
	Amikacin	<i>eis</i>
	Fluoroquinolones	<i>gyrA, gyrB</i>
Novel anti-tuberculosis drugs (5)	Delamanid	<i>gbiA</i>
	Bedaquiline	<i>Rv0678</i>
	Linezolid	<i>rplC</i>
	Capreomycin	<i>tlyA</i>
	Moxifloxacin	<i>gyrB</i>

## ◆ Target Customer

Target Customer Type
● Suspected tuberculosis patient
● Suspected tuberculous pleurisy patient
● Suspected extra-pulmonary tuberculosis patient
● Re-treatment patients with tuberculosis
● Suspected NTM patient
● Multi-drug resistant tuberculosis patient

## ◆ Data Performance

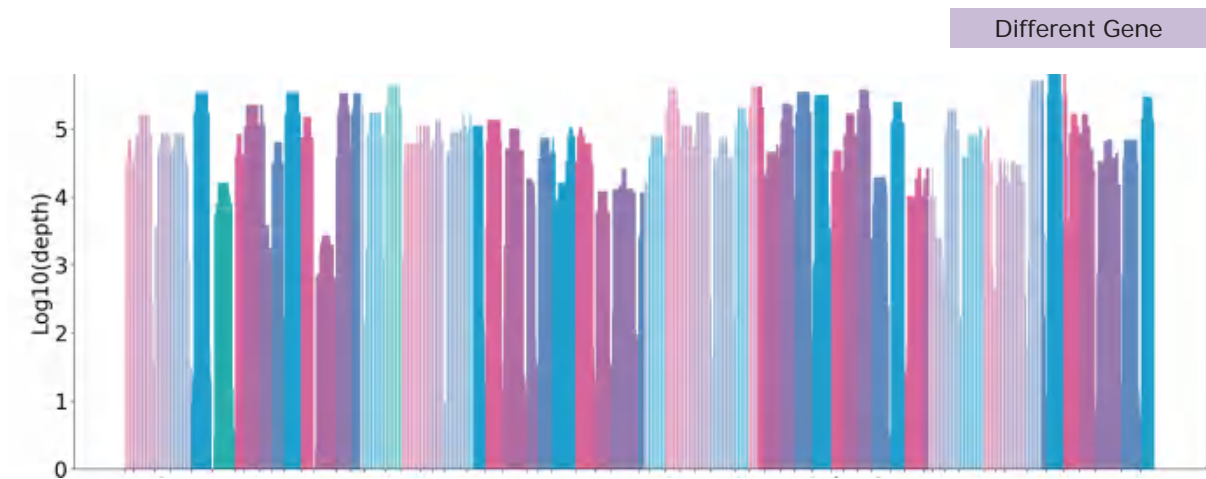


Figure 1: Sequencing depth of each targeted region of sputum samples

Result: The coverage depth are higher than 300X among 95% targeted regions.

## ◆ Application: Clinical Sample Case

Sample type	Sputum samples from one TB patient
Detection method	tNGS VS qPCR
Validation method	Drug sensitivity test(MIC)
Results	tNGS found the drug-resistant mutation earlier than qPCR
Variation information	rpob, c.1334A>G, p.His445Arg
Depth & VAF	869X, 87%
Drug resistance type	Rifampicin resistance
WHO evidence	Associated with Resistance

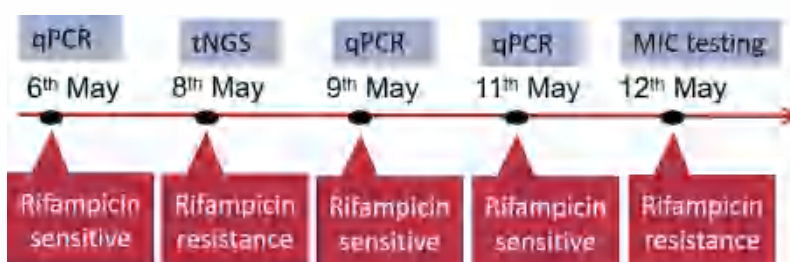


Figure 2: Detection timeline of the clinical sample



Figure 3: tNGS testing result

**Conclusion:** The data analysis results showed that using tNGS method to do the TB drug resistance detection is more sensitive and accurate than traditional qPCR detection method (figure 2 and 3).

## ◆ Product Advantage

### High efficient DNA extraction technique for Mycobacterium:



The self-developed extraction reagent can directly extract Mycobacterium tuberculosis DNA from sputum samples as low as 200  $\mu$ L volume.

### Two-step method with ultra-low input volume for rapid library preparation:



Easy to operate and can be combined with the automation platform to do the library preparation. Could quick test 16 TB related drugs, including rifampicin and isoniazid.

### Release your sequencing speed with more flexible and accurate:



Using the self-developed FASTASeq 300\* sequencing platform and premixed reagents to make amplification and sequencing integrated, achieve more stable data and faster delivery speed.

### Provide completely end-to-end solution:



Using the digital platform to manage sample information more efficiently; One-click data analysis process are easy for users to get quick start.

## ◆ Summary

- ✓ TB is a leading infectious disease killer that causes significant global morbidity and mortality. The evolving resistance of Mtb to multiple anti-TB drugs has complicated eradication efforts.
- ✓ Traditional TB detection methods involve long culture times or fail to characterize the full scope of drug resistance profiles, thereby delaying or limiting the information available to combat the disease.
- ✓ NGS provides flexibility for both rapid characterization of targeted regions and broad surveillance of whole genomes for drug resistance profiling and detection of new mutations.
- ✓ GeneMind tNGS method is backed by several clinical partners, with a shared goal to fight TB.

\*Unless otherwise informed, GeneMind sequencing platform and related sequencing reagents are not available in the USA, Canada, Australia, Japan, Singapore, Western Europe and Nordic countries yet.

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