combine the analysis of social and economic conditions, clinical conditions, drug effects and genetic testing simultaneously. Only in this way can the risk of treatment failure for drug-resistant tuberculosis be predicted more comprehensively and reduced.

6 The Relationship Between the Genetic Background of Individuals and Treatment Failure

6.1 Key genetic variations identified in typical cases

The genes responsible for drug metabolism are different from those related to immunity, which have a significant impact on the therapeutic effect of drug-resistant tuberculosis (DR-TB). For instance, if genes such as cytochrome P450 (CYP) and N-acetyltransferase 2 (NAT2) change, it may alter the metabolic rate of major anti-tuberculosis drugs, thereby affecting the treatment outcome and possibly causing varying degrees of side effects. Studies on Chinese people have found that some *CYP2E1* gene types have no significant association with the incidence of liver injury. In contrast, the relationship between the drug transport gene *ABCG2* and the risk of liver injury and changes in serum enzyme indicators caused by anti-tuberculosis drugs is much clearer.

Genes related to immune regulation can also affect the treatment response and the ability to eliminate bacteria. If genes related to the PI3K/AKT signaling pathway mutate, it may make macrophages difficult to be fully activated and weaken their bactericidal ability. As a result, the risk of tuberculosis will increase (Wu et al., 2023). In addition, variations at the rs7568402 site of the immune checkpoint molecule PDCD1 (also known as PD-1) can also increase the risk of tuberculosis. This indicates that abnormal immune function may lead to more difficult clearance of bacteria and persistent infection (Wang et al., 2021). Changes in genes related to drug metabolism and transport as well as immune-related genes may interact with each other to jointly determine the therapeutic effect. These genes can also serve as candidate biomarkers for clinical stratified risk assessment.

6.2 The relationship between genotype and drug blood concentration/adverse reactions

The absorption and utilization of anti-tuberculosis drugs in the body and their toxic and side effects are closely related to genetic variations that affect the activity of metabolic enzymes and the drug transport capacity. Take the NAT2 gene as an example. People carrying the slow-metabolism type gene usually have a higher concentration of isoniazid in their blood, and their risk of liver damage also increases. For people carrying fast-metabolizing type genes, the concentration of the drug in their bodies may not meet the therapeutic requirements, thereby reducing the effect of eliminating bacteria. During the metabolism of drugs such as rifampicin and pyrazinamide, variations in the *CYP2E1* and *CYP3A4* genes can also cause differences in drug concentrations among patients with different genotypes, leading to situations such as drug accumulation in the body or rapid excretion. Pharmacogenomic studies also support this conclusion, indicating that variations in the *CYP* gene can simultaneously affect the efficacy and safety of anti-tuberculosis treatment regimens (Yang and Wang, 2025).

Genetic differences related to drug transport can significantly affect the distribution of drugs in the body, making people more prone to drug poisoning. Patients with specific *ABCG2* gene variations may be more prone to accumulate toxic metabolites in the liver, thus having a higher risk of liver damage and possibly leading to elevated alkaline phosphatase. Some immune-related variations in the vitamin D receptor (VDR) gene can also alter the strength of the immune response. In the Asian population, certain genetic types not only increase the risk of tuberculosis but may also reduce the probability of recovery after treatment (Li et al., 2022). The genes of different patients vary, which not only affect the metabolism and transport of drugs but also influence the process by which drugs take effect by altering immune function, ultimately determining the treatment outcome of drug-resistant tuberculosis.

6.3 The relationship between genotype and treatment outcomes

When immune-related genes change, it will affect the treatment effect of tuberculosis. Specifically, the tuberculosis bacteria in the sputum cannot turn negative for a long time, or the speed of turning negative is extremely slow, or it will recur after being cured. Some immune genes mutate, which may reduce the body's ability to eliminate bacteria, making it even more difficult to completely eradicate them. Therefore, even with the standard chemotherapy regimen, patients with relatively weak immune function may not achieve the desired therapeutic effect (Wang et al., 2021; Wu et al., 2023). Mutations in the *VDR* gene may increase the risk of