medication is not adjusted based on the results of the drug sensitivity test, or if the medication combination is unreasonable and other non-standard treatment plans are adopted, it will directly reduce the treatment effect and may also make the drug resistance problem more serious (Kherabi et al., 2025).

HIV infection, diabetes, malnutrition and other conditions all increase the risk of treatment failure and death. Among them, patients who are simultaneously infected with HIV often have a relatively low chance of successful treatment due to poor immune system function and possible mutual influence among different drugs. In addition, factors such as excessive alcohol consumption, smoking, advanced age, and previous tuberculosis may also prevent patients from taking medicine on time or affect their overall health, thereby leading to poorer treatment outcomes (Feng et al., 2025; Li et al., 2025). Poverty and insufficient medical resources will make these risks more obvious. Therefore, it is necessary to combine medical assistance with social support to provide patients with more comprehensive help (Bartholomay et al., 2021).

2.3 Significant individual differences in clinical practice and their significance

Even if there are unified treatment standards, the symptoms and treatment outcomes of patients with multidrug-resistant tuberculosis may still vary greatly. These differences are usually associated with many factors (Kherabi et al., 2025). During the medical treatment process, even if patients have similar drug resistance and take the same medications, the final treatment outcomes may still vary. This indicates that some factors that cannot be directly observed (such as genetic conditions, the body's immune response, etc.) may be crucial (Li et al., 2025).

This situation where everyone is different indicates that it is not feasible to treat all patients with exactly the same treatment plan. When formulating the treatment plan, the patient's own risk factors such as genetic characteristics should be considered to make the treatment more tailored to the individual situation (Kherabi et al., 2025; Li et al., 2025). To alleviate the troubles caused by the failure of treatment for multidrug-resistant tuberculosis, molecular diagnosis, personalized treatment and social assistance should be combined to better solve the problems of different patients.

3 Key Genes and Pathways Influencing Treatment Outcomes

3.1 Drug metabolism genes and their polymorphisms

Drug metabolism plays a core role in determining the pharmacokinetics and therapeutic effects of anti-tuberculosis drugs, and genetic variations encoding metabolic enzymes are an important source of individual differences in treatment outcomes, especially more prominent in patients with drug-resistant tuberculosis. Among them, the polymorphisms of the N-acetyltransferase 2 (NAT2) and cytochrome P450 (CYP) gene families have been studied most deeply. The NAT2 acetylation phenotype directly affects the metabolism of isoniazid (INH) : those with slow acetylation are more likely to have higher plasma INH levels and an increased risk of hepatotoxicity, while those with rapid acetylation may have insufficient drug exposure, thereby reducing efficacy and promoting drug resistance. Meanwhile, polymorphisms of genes such as *CYP2E1*, *CYP2C19* and *CYP3A4* can alter the metabolic clearance rates of various anti-tuberculosis drugs, thereby affecting the balance between efficacy and toxicity. Studies of populations in Indonesia and China suggest that *CYP2E1* and NAT2 polymorphisms are closely related to drug-induced liver injury during treatment, indicating that these genetic differences will shape the treatment outcomes of drug-resistant tuberculosis to a certain extent.

The impact of the differences in the *CYP450* gene is not only reflected in the "rate of drug metabolism", but also affects the overall therapeutic effect by altering the interactions between drugs. Enzymes like *CYP3A4* and *CYP2D6* are involved in the metabolism of both the body's own substances and various substances that enter the body from the outside. So, when they encounter other drugs being taken simultaneously or when their own genes undergo mutations, leading to inhibition or enhancement of activity, it may cause significant changes in the concentration of the drugs in the body and their toxic and side effects. Studies have mentioned that even components in daily diet (such as polyphenols in herbal tea) may inhibit the metabolic processes involved in *CYP3A4*, thereby indirectly affecting the metabolism of anti-tuberculosis drugs in the body. Therefore, the differences in these metabolism-related genes are not only related to whether patients are prone to adverse drug reactions, but also closely associated with poor treatment outcomes and the emergence of drug resistance.