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Association between *TXNRD1* polymorphisms and anti-tuberculosis drug-induced hepatotoxicity in a prospective study

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ABSTRACT. Anti-tuberculosis drug-induced hepatotoxicity (ATDH) is a serious adverse reaction to anti-tuberculosis (TB) treatment. Thioredoxin reductase 1 (TXNRD1), encoded by the *TXNRD1* gene, is an important enzyme involved in oxidant challenge. TXNRD1 plays a key role in regulating cell growth and transformation, and protects cells against oxidative damage. We investigated the association between *TXNRD1* polymorphisms and ATDH susceptibility. In this prospective study, 280 newly diagnosed TB patients were followed-up for 3 months after beginning anti-TB therapy. Tag single-nucleotide polymorphisms (tag-SNPs) of *TXNRD1* were selected using Haploview 4.2 based on

the HapMap database of the Chinese Han in Beijing (CHB) panel. Genotyping was performed using the MassARRAY platform. Of the 280 patients enrolled in this study, 33 were lost to follow-up, 24 had ATDH, and 223 were free from ATDH. After adjusting for sex, age, smoking status, and body mass index, there were no significant differences in the allele and genotype frequency distributions of *TXNRD1* SNPs between the ATDH and non-ATDH groups (all $P > 0.05$). The haplotype analysis showed that haplotype TCAGCC was associated with an increased risk of ATDH susceptibility [P = 0.024, OR (95%CI) = 6.273 (1.023-38.485)]. Further stratified analyses showed that the haplotype TCAGCC was associated with ATDH susceptibility in female subjects [P = 0.036, OR (95%CI) = 5.711 (0.917-35.560)] and non-smokers [P = 0.029, OR (95%CI) = 6.008 (0.971-37.158)]. Our results suggest that *TXNRD1* variants may favor ATDH susceptibility in females and non-smokers. Further studies are required to verify this association.

Key words: Thioredoxin reductase 1; *TXNRD1*; Polymorphism; Anti-tuberculosis drug-induced hepatotoxicity; ATDH