

## Publication

## Association of the glucocorticoid receptor D641V variant with steroid-resistant asthma: a case-control study

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**OBJECTIVES:** Several mutations of the glucocorticoid receptor (GR) gene cause malfunction of the protein, resulting in steroid resistance. In diseases other than asthma, the GR variants I559N, D641V, and V729I have been linked to steroid resistance. The aim of this study was to evaluate the link of these GR variants in steroid-resistant (SR) asthma in the Chinese Han population. **METHODS:** GR polymorphisms were determined in 64 SR asthma patients, 217 steroid-sensitive (SS) asthma patients and 221 healthy control (CTR) individuals. The analysis of the GR variants was performed using PCR-sequence specific primers according to the European Molecular Biology Laboratory database (NC\_000005.8). In addition, ligand binding and serum cortisol levels were determined. **RESULTS:** Compared with SS asthma patients and CTRs, a significant lower frequency of the GR D641V variant AA genotype ( $P=0.003$ ,  $0.014$ , respectively) and the A allele ( $P=0.001$ ,  $0.009$ , respectively) was found in SR asthma patients. Furthermore, the equilibrium dissociation constant ( $K_d$ ) of GR ligand binding in SR asthma patients with the GR D641V variant AA genotype was significantly lower compared with the AT or the TT genotype carriers ( $P=0.006$ ,  $0.016$ , respectively). There was no significant difference between the I559N and V729I GR variants on comparing SR asthma patients with SS asthma patients or CTRs. **CONCLUSION:** This study suggests that the D641V variant of the GR is probably associated with SR asthma in the Chinese Han population.

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