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Genetic Variations of Multidrug Resistance Protein 2 Associated with Adverse Drug Reactions of Valproic Acid in Epilepsy Patients

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Multidrug resistance-associated protein 2 (MRP2, ABCC2), is a member of ATP-binding cassette (A-BC) transporter superfamily, and plays an important role in drug efflux and disposition in the central nervous system. Therefore, polymorphisms and mutations in the genes coding MRP2 protein are important candidates to cause altered responses of anti-epileptic medications. In this study, we have investigated the association between polymorphisms of MRP2 and the individual drug adverse reactions, especially of valproic acid. One hundred and seventy one patients were divided into two groups according to the CNS adverse drug reactions; those who experienced the adverse drug reactions of valproic acid (ADR; n=42) and those who did not (non-ADR; n=129). It was found that MRP2 variants in the promoter region, g.−1,774DelG and g.−24C>T showed a differential association with the CNS adverse drug reactions caused by valproic acid (P=0.005, P=0.008, respectively). Accordingly, these variations altered the MRP2 promoter activities in reporter assays. The above results suggest that polymorphisms in the human MRP2 gene may be associated with adverse drug reactions of valproic acid medication in epilepsy patients.

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