Effects of CYP2C9 Genetic Polymorphism on the Pharmacokinetics of Irbesartan
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Purpose
Irbesartan is an angiotensin II antagonist that selectively blocks the binding of angiotensin II to the AT\textsubscript{1} receptor, used for the treatment of essential hypertension. Irbesartan is extensively metabolized to inactive metabolite by CYP2C9, one of the highly polymorphic drug metabolizing enzymes. In addition to CYP2C9*2 and *3 alleles, both in vitro and in vivo studies showed that CYP2C9*13 allele also shows impaired activity towards a number of substrates. It is reported that CYP2C9*13 allele has been only detected at a low frequencies in East Asians, including Korean, while not detected in other populations. We investigated the effects of CYP2C9*13 allele on the pharmacokinetics of irbesartan.

Methods
Eighteen subjects were recruited and divided into two different groups according to CYP2C9 genotype, CYP2C9*1/*1 (n=12) and CYP2C9*1/*13 (n=6). Each subject received a 150 mg oral dose of irbesartan. Plasma concentrations of irbesartan were determined by HPLC method with fluorescence detection.

Results
Subjects with CYP2C9*1/*13 genotype showed significantly higher C\textsubscript{max} (P<0.01) and AUC (P<0.001) of irbesartan than those in subjects with CYP2C9*1/*1 genotype. Elimination half-life (t\textsubscript{1/2}) of irbesartan in CYP2C9*1/*13 group was also significantly longer than that in CYP2C9*1/*1 group (P<0.001). Oral clearance (CL/F) of irbesartan in CYP2C9*1/*13 group was significantly lower than that in CYP2C9*1/*1 group (P=0.002).

Conclusion
In conclusion, CYP2C9*13 allele has an impact on the metabolism of irbesartan.