

# **Genes-4U**

## **Cytochrom P450 CYP2C9\*3 (Ile359Leu)**

Cytochrome P450 2C9 (CYP2C9) catalysis the metabolism of important drugs such as phenytoin, S-warfarin, tolbutamide, losartan, torasemide, and nonsteroidal anti-inflammatory drugs. A functional polymorphism of the CYP2C9 gene has been described. The variant alleles include CYP2C9\*2 having a point mutation in exon 3 causing an Arg144Cys exchange, and CYP2C9\*3 with a point mutation in exon 7 resulting in an Ile359Leu exchange. The frequencies of the CYP2C9\*1, CYP2C9\*2 and CYP2C9\*3 alleles are about 0.8, 0.1, and 0.1, respectively. The present data suggest that the incidence of the Leu359 allelic variant of CYP2C9 may account for the occurrence of poor metabolizers of phenytoin, S-warfarin, tolbutamide, losartan, torasemide, and nonsteroidal anti-inflammatory drugs. Because (S)-warfarin has a greater anticoagulant potency than its (R)-congener, the genetic polymorphism of CYP2C9 may partly account for the large interpatient variability in therapeutic dosages of warfarin.

### References

Comparative studies on the catalytic roles of cytochrome P450 2C9 and its Cys- and Leu-variants in the oxidation of warfarin, flurbiprofen, and diclofenac by human liver microsomes. Yamazaki H et al. *Biochem Pharmacol* 1998 Jul 15;56(2):243-51

The effects of genetic polymorphisms of CYP2C9 and CYP2C19 on phenytoin metabolism in Japanese adult patients with epilepsy: studies in stereoselective hydroxylation and population pharmacokinetics. Mamiya K et al. *Epilepsia* 1998 Dec;39(12):1317-23