

## Prescription Drug Reaction Testing Physician Interpretive Comments

The information below can help you understand and apply the results of the **DNA Prescription Drug Reaction Test for CYP1A2** currently offered by Genelex.

### CYP1A2 Interpretation

CYP1A2 is primarily responsible for the metabolism of some important medications, including theophylline, clozapine, and caffeine. CYP1A2 is also involved in the metabolic activation of carcinogens from chemical toxins. There is considerable variation in 1A2 metabolic activity due to genetic factors, environmental factors, and drug-drug interactions. CYP1A2 is both inducible and can be inhibited, “turned on or off” by many medications and food-drug interactions. Fluoroquinolones, for example, are metabolized by and inhibit the enzyme CYP1A2. This can prevent the metabolism of concomitant medications such as theophylline and caffeine, causing excess central nervous system side effects and cardiac stimulation. Conversely, smoking may induce CYP1A2, resulting in enhanced metabolism of 1A2 substrates and the potential of sub-therapeutic response. The variation of the intensity of CYP1A2 activity could result in increased or decreased capacity to activate substrates.

Genetic polymorphisms in the CYP1A2 gene influence the magnitude of CYP1A2 induction. Two important polymorphisms that cause functional changes in enzymatic activity have been identified in the CYP1A2\*1 allele. The **CYP1A2\*1C** allele is the result of a single point mutation (-3860 G>A) in the 5'-flanking region of human CYP1A2 gene. This allele is associated with decreased CYP1A2 metabolic activity (measured in terms of the rate of caffeine metabolism) in comparison to the wild-type CYP1A2\*1A allele. The **CYP1A2\*1F** allele is the result of a single point mutation (-163 C>A) in intron 1, downstream of the first transcribed nucleotide of the human CYP1A2 gene. This allele has increased induction particularly in smokers (measured in terms of the rate of caffeine metabolism) in comparison to the wild-type CYP1A2\*1A allele. The distribution of CYP1A2 genotypes at this nucleotide position (-163) is as follows: \*1F/\*1F (nucleotide sequence A/A) ~ 46 %; \*1A/\*1F (nucleotide sequence C/A) ~ 44%; and \*1A/\*1A (nucleotide sequence C/C) ~ 10%, indicating that high induction is the most common phenotype.

### Key Terms

**Substrates** - If a drug is listed as a substrate of a pathway, that is the main pathway for metabolism.

**Inhibitor** - If a drug is listed as an inhibitor of a pathway, it reduces or blocks the ability of the pathway to metabolize the substrates.

**Inducer** - If a drug is listed as an inducer of a pathway, it will increase the ability of the pathway to metabolize the substrates.

### References

1. Chida M et al., Jpn J Cancer Res 1999; 90:899-902.
2. Sachse C et al., Br J Clin Pharmacol 1999; 47(4):445-9.
3. Nakajima M et al., J Biochem (Tokyo) 1999; 125(4):803-8.
4. Hamdy SI et al., Br J Clin Pharmacol 2003; 55:321-324.
5. Eap CB et al., J Clin Psychopharmacol 2004; 24(2):214-219.

**For immediate consultation Call 877-431-4362**

Hours 7:00 AM to 6:00 PM PST, 10:00 AM to 9:00 PM EST, fax 206-219-4000,

Genelex Corporation, 3000 First Avenue, Suite One, Seattle, WA 98121

E-mail: [info@genelex.com](mailto:info@genelex.com) Web: [www.genelex.com](http://www.genelex.com); **Se habla español**, ©2004 Genelex Corporation