

## P450 2D6 CYTOCHROME (CYP2D6) GENOTYPING

## CLINICAL RELEVANCE

- CYP2D6 metabolizes more than 25% of all drugs, including tamoxifen, many antidepressants, antipsychotics, beta-blockers, and opioids. Detecting variants of the CYP2D6 gene that cause altered enzymatic activity can identify patients who may be at increased risk of having adverse drug reactions or therapeutic failure to standard dosages of CYP2D6 substrates. Medications which require activation or inactivation by CYP2D6 should be used with caution in patients with CYP2D6 variants.

## PHENOTYPE CATEGORIES

- **Extensive metabolizers (EM)** represent the norm for metabolic capacity. Genotypes consistent with the EM phenotype include two active CYP2D6 alleles or one active and one partially active CYP2D6 allele.
- **Intermediate metabolizers (IM)** represent reduced metabolic capacity. Genotypes consistent with the IM phenotype are those with one active and one inactive CYP2D6 allele, one inactive and one partially active CYP2D6 allele, or two partially active CYP2D6 alleles.
- **Poor metabolizers (PM)** are at increased risk of drug-induced side effects due to diminished drug elimination or lack of therapeutic effect resulting from failure to generate the active form of the drug. Genotypes consistent with the PM phenotype are those with no active CYP2D6 genes.
- **Ultra-extensive metabolizers (UM)** exhibit higher than average rates of metabolism. UMs are at increased risk of therapeutic failure due to increased drug elimination and thus may require an increased dosage of medications that are inactivated by CYP2D6. Alternatively, UMs may also be at increased risk of drug-induced side effects due to increased exposure to active drug metabolites, in which case they may require lower than average doses. Genotypes consistent with UM phenotype include three or more active CYP2D6 alleles due to duplication of an active allele.

## ALLELES DETECTED

- **Active alleles:** CYP2D6 \*1, \*2
- **Partially active alleles:** CYP2D6 \*9, \*10, \*17, \*41
- **Inactive alleles:** CYP2D6 \*3, \*4, \*5 (deletion), \*6, \*7, \*8, \*11, \*12, \*14, \*15
- **Gene Duplication:** CYP2D6 \*1, \*2, \*4, \*10, \*41

