CYP2C19 SEQUENCE VARIANTS ASSOCIATED WITH RESISTANCE TO CLOPIDOGREL (PLAVIX)

The UNC Molecular Genetics Laboratory performs molecular testing to detect cytochrome P450 2C19 (CYP2C19) sequence variants associated with resistance to clopidogrel (Plavix) anti-platelet therapy and increased cardiovascular morbidity and mortality.

**Background:** Clopidogrel (Plavix) is an anti-platelet agent used to treat coronary artery disease, peripheral vascular disease and cerebrovascular disease. A significant proportion of patients is at risk for myocardial infarction, stent thrombosis, or stroke due to insufficient clopidogrel-induced platelet inhibition. Clopidogrel is metabolized by CYP2C19 and other liver enzymes to an active form. Genetic variants of CYP2C19 associated with altered CYP2C19 activity have been identified and are relatively common in most populations. Individuals with loss of function variants CYP2C19*2 or CYP2C19*3 (~15% of the population) are at increased risk for thrombotic cardiovascular events due to decreased drug efficacy. In contrast, the fast (ultra)-metabolizing variant CYP2C19*17 (in ~20% of the population) is associated with increased drug activation and increased risk of bleeding. The US FDA has recently recommended considering a higher dose of clopidogrel or use of alternative therapy such as Prasugrel in CYP2C19 poor metabolizers who are homozygous for loss of function alleles.

**Clinical Indications for CYP2C19 polymorphism testing:** Testing is recommended in patients who are being considered for clopidogrel antiplatelet therapy or who are already on this medication.

**Laboratory Testing for CYP2C19 polymorphisms:** The preferred sample is 2mL of EDTA anticoagulated blood (lavender-top), which may be refrigerated up to 48 hours before analysis. Genomic DNA is extracted and CYP2C19 *2, *3 and *17 targets are PCR amplified and detected by TaqMan probes using an ABI real-time PCR instrument. Allelic discrimination is facilitated by software analysis of the fluorescence data. Homozygous or heterozygous presence of three common CYP2C19 genotype variants (*2, *3, *17) is reported. A pathologist interprets the clinical significance of variants associated with clopidogrel response.

**References:**

**Questions?** Call the Molecular Genetics Lab at (919) 966-4408 or email Dr. Karen Weck at: kweck@unch.unc.edu.