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From pharmacognomics testing to personalized medicine: Establishing CYP2D6 reference samples by multiple validated genotyping platforms

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Abstract

Cytochrome P450 2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6, or CYP2D6) is one of the most important drug-metabolizing enzymes involved in the metabolism of approximately one quarter of the mostly prescribed medications, including multiple anticancer drugs like Tamoxifen, which is a selective estrogen receptor (ER) modulator widely used for the treatment and prevention of recurrence for breast cancer patients showing positive hormone receptors. The CYP2D6 gene is highly polymorphic and its genetic polymorphism significantly affects its enzymatic activity. Due to the clinical significance of the medications metabolized by CYP2D6, it is critical in a clinical setting to get accurate estimation for CYP2D6 metabolic activity based on the determination of CYP2D6 genotyping results. Here, we have applied multiple genotyping/sequencing methodologies to get accurate CYP2D6 genotype results of 48 Hapmap samples. Furthermore, we also confirmed the utility of our genotyping methodologies for CYP2D6 phenotype prediction. We genotyped 51 liver microsomes from healthy Caucasian donors and the predicted phenotyping results from our genotyping data matched well with the *ex vivo* phenotyping results of Endoxifen formation from Tamoxifen metabolism. In the future, these 48 publicly available Hapmap samples combined with our validated CYP2D6 genotyping methodologies can be used for assay development, validation, quality control, and proficiency testing for any CYP2D6 genotyping projects, particularly for those projects needed to be done in a Clinical Laboratory Improvement Amendments (CLIA) setting, like The 1200 Patients Project currently being conducted in the University of Chicago.

Biography

Hua Fang obtained her Bachelor in Pharmacy degree at Zhejiang University in China in 2005, and subsequently completed her Ph.D. at University of Southern California with a focus on Cancer Biology and Pharmacology in 2012. During her Ph.D. training, Hua Fang has won many trainee awards, including the Best PhD Graduate Award from University of Southern California, American Association for Cancer Research Bristol-Myers-Squibb Oncology Scholar-in-Training Award, The Saban Research Institute of Children's Hospital Los Angeles Pre-Doctoral Fellowship, and University of Southern California Best Poster Presentation Award. She started her post-doctoral training as a Clinical Pharmacology and Pharmacogenomics Fellow at University of Chicago since Aug. 2012, and she is now conducting translational research in cancer pharmacogenomics and immunogenomics areas.