Pharmacogenetics, Pharmacogenomics, Precision Medicine

AB130. Comprehensive analysis of *CYP2D6* and copy number variants using reverse-hybridization and real-time PCR-based assays

Anne Berndt, Christian Oberkanins, Helene Puehringer

ViennaLab Diagnostics, Wien, Austria

Background: The cytochrome P450 2D6 (CYP2D6) is an important liver enzyme involved in the metabolism of up to 25% of clinically used drugs. The *CYP2D6* gene is highly polymorphic, with numerous (sub)variants described in the Human Cytochrome P450 Database (www.cypalleles.ki.se). While the most frequent allelic variations are caused by single nucleotide polymorphisms and small insertions/deletions, highly homologous regions in the *CYP2D6* gene locus facilitate unequal cross-over, leading to large deletions, duplications and gene conversions.

Methods: We developed a reverse-hybridization assay (PGX-CYP2D6 XL StripAssay) for the simultaneous detection of 19 sequence variations in the *CYP2D6* gene, which define the most prevalent alleles impacting enzyme activity in Caucasians. For the detection of copy number variations, a real-time PCR based assay (CYP2D6 RealFast CNV Assay) was established. The StripAssay and real-time PCR assay were validated on 118 and 98 samples, respectively.

Results: The PGX-CYP2D6 XL StripAssay correctly identified allelic variants with normal (*1, *2, *35, *39), reduced (*9, *10, *17, *29, *41) and no (*3 to *8, *11, *12, *14, *15, *40, *58) enzyme activity, hence allowing the classification of individuals into extensive (EM), intermediate (IM) and poor (PM) metabolizers. In addition, ultrarapid (UM) metabolizers and *CYP2D6**5 carriers can be identified by quantifying their abnormal copy number status using the CYP2D6 RealFast CNV Assay. Both assays demonstrated a test accuracy of >0.99.

Conclusions: The metabolizer phenotype of patients treated with CYP2D6 substrates can be accurately determined by the combined use of PGX-CYP2D6 XL StripAssay and CYP2D6 RealFast CNV Assay.

Keywords: *CYP2D6*; cytochrome P450; drug metabolizer; genotyping

doi: 10.21037/atm.2017.s130

Cite this abstract as: Berndt A, Oberkanins C, Puehringer H. Comprehensive analysis of CYP2D6 and copy number variants using reverse-hybridization and real-time PCR-based assays. Ann Transl Med 2017;5(Suppl 2):AB130. doi: 10.21037/atm.2017.s130

