

## Role of pharmacogenetics in adverse drug reactions

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Significant advances have been made in understanding the genetic bases for inter-subject variability in therapeutic outcomes, including adverse drug reactions (ADRs) and drug-drug interactions (DDIs). Genetic differences impact the nature of drug-receptor interaction and the resulting pharmacodynamics (PD) or toxicodynamics (TD) of a drug. Similarly, genetic-based differences in the expression and activity of drug metabolizing enzymes and drug transporters contribute to the inter-subject variability in the pharmacokinetics (PK) and toxicokinetics (TK) of a drug. Some examples that underscore the importance of pharmacogenetics include: a) A variant form of the enzyme glucose-6-phosphate dehydrogenase leading to serious toxicity of hemolytic anemia from the antimalarial drug primaquine; b) Certain genotypes of ATP-binding cassette (ABC) transporters additively increased irinotecan-induced neutropenia; and c) Genetic differences in 5-HT<sub>2A</sub> receptors influence clinical response to the antipsychotic clozapine. Thus, pharmacogenetics, the science of the role of genetic makeup in the individual variation in drug response, has the potential to minimize drug toxicities and maximize the chances of therapeutic efficacy. In 2005, FDA approved Roche's AmpliChip<sup>TM</sup> CYP450 Test for rapid genotyping variants of cytochrome-P450 (CYP) enzymes such as CYP2D6 and CYP2C19. However, translation of pharmacogenetics into clinical settings has been a very slow process due to a number of confounding factors. These include a lack of clear delineation of how variable expression of a single or a cluster of related gene impact clinical outcome and lack of validated strategies for dose modifications. This seminar will provide an update on some of the advances in the field with a focus on the complexities and success stories.

### Biography

Nimita Dave is currently a doctoral candidate at College of Pharmacy, University of Cincinnati. She has Bachelors in Pharmaceutical Sciences from University Institute of Chemical Technology, Mumbai, India and Masters in Chemistry from Eastern Michigan University. Nimita has acquired significant expertise in the pharmacokinetics, pharmacodynamics, drug metabolism and drug transport studies with a focus on the brain transport of anti-tumor drugs. She also has a strong background in functional genomics and clinical pharmacology with emphasis on factors contributing to inter-subject variability in pharmacological or toxicological outcome of drug therapy.

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