Pharmacogenetics – The Future is Now!

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Variability in response is a major limitation to the safe and effective use of drug therapy in perioperative care. For example, the same drugs used to treat heart rhythm disturbances may in some cases elicit more malignant, life-threatening arrhythmias. Recently, advances in our understanding of variable drug response have arisen from the identification of mutations in genes that evoke rare syndromes, such as the congenital long QT syndrome, that occur in the absence of drug therapy. Nonetheless, while rare mutations in these genes elicit profound disease, it is now clear that far more common mutations (know as single nucleotide polymorphisms, or SNPs) evoke only subtle changes in the protein-products of the same genes. These SNPs render mild disease, or even a loss of functional reserve, that create the potential for drug-induced adverse events, such as Torsades de Pointes. As such, the long QT syndrome serves as a model for understanding a variety of interactions between drugs and common variations in genetic sequence, a discipline broadly referred to as pharmacogenomics.

Identification of mutations in genes that underlie rare syndromes allow the use of simple model systems, such as *C. elegans*, to identify new modulator genes that may carry common SNPs evoking variable drug response through the same mechanistic pathway. These approaches are leading to the assembly of a more complete database of the common genetic variants that elicit variable drug response in perioperative care, and will eventually allow prospective therapeutic decisions based upon individual DNA fingerprints.