Spotlight on Dr. Jie An: a Pharmacogenomics and Personalized Medicine Expert

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In this issue, Molecular and Cellular Pharmacology profiles Jie An, Ph.D. and her expertise in the fields of pharmacogenomics and personalized medicine. Dr. An is the Assistant Director and Principal Scientist in the Laboratory of Gulfstream Genomics at Gulfstream Diagnostics, Dallas, Texas, USA. Dr. An is an expert in the fields of pharmacogenomics and personalized medicine. She is a founding member of Gulfstream Genomics and devotes her efforts to study the influences of genetic variability on drug response. Dr. An also provides scientific leadership in technical development and clinical implementation of pharmacogenetic testing. Pharmacogenomics and personalized medicine are emerging areas with a limited number of experts. Therefore, Dr. An is among a select few experts of these disciplines. Molecular and Cellular Pharmacology presents her views on the progress of these disciplines in a ‘Question and Answer’ format.

What is pharmacogenetics or pharmacogenomics?

Pharmacogenetics and pharmacogenomics are related terms. Simplistically, pharmacogenomics can be considered a broad term to indicate how genome affects responses to therapeutic agents, and pharmacogenetics can be defined as the study of how individual genes affect a person’s response to drugs. For example, there is a group of genes called pharmacogenes whose translational products are drug metabolizing enzymes and proteins engaged in transport or efflux of drugs. Certain single nucleotide polymorphisms (SNPs) in these genes can change their enzymatic activity or the drug transport/efflux function.

What is precision medicine and how does it differ from personalized medicine?

‘Precision medicine’ and ‘personalized medicine’ are terms with similar meanings and often used interchangeably. According to the National Academy of Sciences, precision medicine is defined as “the use of genomic, epigenomic, exposure and other data to define individual patterns of disease, potentially leading to better individual treatment.” According to the National Research Council, precision medicine focuses on “identifying which approaches will be effective for which patients based on genetic, environmental, and lifestyle factors”.

What does pharmacogenetic testing do and how does it relate to personalized medicine?

The pharmacogenomics/pharmacogenetics principles are tightly linked to precision/personalized medicine. Pharmacogenetic tests can detect the SNPs in important pharmacogenes and provide valuable information to physicians about how a patient will respond to one or many drugs based on patient’s specific genetic makeup. Thus, pharmacogenetic testing assists physicians in prescribing the right medication with right dose at the right time, all based on individual’s genotypes and phenotypes of the pharmacogenes.

How does pharmacogenetic testing prevent adverse drug reactions due to prescription medication?

All prescription medications are associated with risks of adverse drug reactions (ADRs). A large number of ADRs are life threatening or fatal. In addition to pain and suffering, and loss of life, the health care cost due to ADRs is very high. The FDA estimates the cost due to ADRs to be in the range of $136 billion per year and this figure is only for the
USA. Thus, morbidity and mortality due to ADRs are high and can be prevented by pharmacogentic testing. Several pharmacogentic tests are now developed that predict genetic variations and drug response.

For example, warfarin (Coumadin) is an anticoagulant in clinical use that has proven to be an important drug in the prevention of thromboembolic events. However, it is known that people exhibit variable response to warfarin, and due to individuals' variability, its use can lead to ADRs. Two genes including CYP2C9 and VKORC1 have variants that could be responsible for a large number of cases for variability in warfarin dosing. CYP2C9 is responsible for clearing the active form of warfarin, whereas VKORC1 is a target for warfarin’s blood thinning effects. Therefore, the knowledge of CYP2C9 and VKORC1 variants that facilitates pharmacogentic testing to determine these variants can help the healthcare providers to be fully informed about the bleeding risks associated with warfarin use among different individuals. Now we have a newer class of anticoagulants including apixaban, dabigatran and rivaroxaban and these can be used instead of warfarin if the situation warrants.

Tamoxifen is another example. It is a component of hormone receptor-positive breast cancer therapy. It is well tolerated and its clinical benefits are well-documented. However, a large number of patients receiving adjuvant tamoxifen either relapse or die due to development of resistance. Tamoxifen is pro-drug that is metabolized by cytochrome P450 (CYP) enzymes particularly CYP2D6 into its active metabolites including 4-hydroxytamoxifen and endoxifen. There are four reported phenotypes of CYP2D6 among Caucasians in relation to drug-oxidation including extensive metabolizer, intermediate metabolizer, poor metabolizer and ultra-rapid metabolizer. These phenotypes result from various alleles and can be determined by genotyping the individual’s DNA. As an example, the poor metabolizer phenotype results from the presence of two nonfunctional alleles. It has been reported that the poor metabolizer and intermediate metabolizer alleles of CYP2D6 are linked to increased recurrence rates. The CYP2D6 gene variants that affect tamoxifen metabolism are expected to diminish tamoxifen efficacy. Thus, pharmacogentic testing to determine allelic variants of CYP2D6 should be beneficial to predict those who will relapse and for those post-menopausal patients alternative medications such as aromatase inhibitors can be used.

Which areas are currently benefiting from pharmacogentic testing and what does the future hold for pharmacogenetics/pharmacogenomics and precision/personalized medicine?

There are several areas currently benefiting from pharmacogenetic testing including cardiology, oncology, psychiatry and pain management to name a few. Pharmacogenetic testing has also started to gain entry into the rural medical practices. However, Pharmacogenomics as a discipline is still evolving. We still need to develop additional pharmacogenetic-based decision support tools for clinical practices and identify more pharmacogenes. I am confident that pharmacogenetics will continue to shape the future of medical practice and eventually all areas of medicine will benefit from it. Evidence-based approaches in prescribing medications will become a routine to ensure personalized care. I am hopeful that in the future, benefits of prescription drugs will be fully realized with no to minimal toxicities and improved clinical outcomes. Ultimately, people will live longer and healthier lives. The future of pharmacogenetics and personalized medicine looks bright.

Conflicts of Interest

Dr. Jie An has no conflicts of interest to declare.