Today's Presentation

Program: Introduction to Pharmacogenomics
Speaker: David Kisor, Pharm.D, Professor and Chair, Pharmaceutical Sciences Director, Manchester University
Attendance: 101
Guests: Jim Stohler, Sue Dillon
Introduced by: Carl Holl
Scribe: Bill Elliott
Editor: Joe Abella

Dr. David Kisor joined the Pharmacy Program in June 2014, and is responsible for facilitating, teaching, scholarly activity, and service in the Department of Pharmaceutical Sciences as Chair. Dr. Kisor came to Manchester University from the Raabe College of Pharmacy at Ohio Northern University. He received his Bachelor of Science degree in Pharmacy from the University of Toledo and his Pharm.D. from The Ohio State University.

Dr. Kisor gave an extremely interesting talk to us today on the topic of pharmacogenomics, (the study of the role of genetics in drug response), and pharmacogenetics (the branch of pharmacology concerned with the effect of specific genetic factors on reactions to specific drugs).
The genetic factors usually involve an SNP (Single Nucleotide Polymorphism) or "SNIP". For years now it has been noted that the molecules used in medical practice had variable effects depending on the individual taking the medication. The study of movement of drugs within the body was called pharmacokinetics. With the human genome project, these individual variations could be associated with specific genetic variations "SNIPS". It was explained that there were several processes involved with proper drug performance. One in particular is proper drug transport to its site of action. An example of this is the transport of statins into the liver cells which depends on the correct architecture of a transport protein in the cell membrane of liver cells. If that protein is distorted, the drug fails to be taken up properly by the liver, and accumulates in the body where it can cause muscle destruction and other problems while, at the same time, it fails to correct the high cholesterol level properly.

Within the body there are metabolizers of drugs. If these metabolizers are genetically altered, the drugs can be rapidly metabolized, causing decreased drug effectiveness as well as a buildup of metabolites in the body which in themselves may be harmful. He gave the example of codeine which can be rapidly metabolized to morphine. In one unfortunate case, a mother was given codeine for pain, and metabolized it to morphine which was excreted in the breast milk, and caused the death of her newborn child. This women's genetic make-up resulted in her being an *ultra-rapid metabolizer* of codeine. The drug can also be poorly metabolized causing an excess of drug in the system resulting in toxicity problems, and requiring a need to decrease drug dosage.
A third way that drugs interact with the body is by blocking receptors. If a receptor is genetically deformed, then the blocking mechanism may be impaired. The example given was antihistamine blockers for various ailments. If these can't bind on the receptor normally, their effectiveness is at least partially neutralized.

Fourthly, enzymes necessary to take a molecule from a precursor form to its bio active form may be abnormal, and the medicine may be totally ineffective. The example here was for Plavix, a common

and expensive drug to prevent vascular thrombosis. Lack of proper anticoagulation can obviously have devastating results. These problems are present across the pharmaceutical spectrum, and involve some of the most prescribed medications. To sort this out, genetic testing will be necessary both for specific treatments, and across the board to identify problems before drugs are considered, or surgery is performed. Infants will likely have their genome taken at birth to identify potential drug interaction problems as well as other inborn errors of metabolism.

Judging from the number of questions from the audience, the talk was of extreme interest and personal pertinence to our members and guests.

Hopefully Dr. Kisor can return next year to finish his talk and update us on new developments.

Dr. Paul Kisor