

Continuing the tutorial series on genetics, genomics and proteomics, Richard M. Weinshilboum, MD, Professor of Medicine and Pharmacology, Mayo Medical School, Rochester spoke on: "Pharmacogenomics: Inheritance and Drug Response". Two medical revolutions converged at the end of the 20th century. A "Therapeutic Revolution" made it possible to develop new forms of drug therapy, while the "Genomic Revolution" made it possible to individualize that therapy on the basis of genetic information, i.e., "Pharmacogenetics". Pharmacogenetics is the study of the role of inheritance in the variation of response to chemicals/drugs. Pharmacogenetics is evolving into pharmacogenomics, which addresses issues like the selection of patients responsive to a particular drug therapy and the avoidance of adverse drug reactions. Numerous patient factors affect individual response to drugs, including genetic makeup, age, gender, underlying disease and drug-drug interactions. Pharmacogenetics targets the role of genetics in the absorption, distribution, metabolism and excretion of drugs, as well as in drug-receptor interactions. Two phases of drug metabolism are of interest; phase 1 consists of oxidation, reduction and hydrolysis reactions while phase 2 involves conjugation reactions. The role of genetics in drug metabolism is well established. An example is the treatment of Acute Lymphocytic Leukemia (ALL) in children with the cytotoxic drug 6-mercaptopurine which in some cases can lead to a toxic response. Pharmacogenomics is addressing the variation in drug metabolism with genetic makeup. For example, the plasma concentration of the antidepressant nortriptyline has been correlated with the number of copies of a specific gene (CYP2D6). From an industrial perspective pharmacogenomics can help identify novel drug targets and guide the drug development process; however it also raises the prospect of market fragmentation and shrinkage as genetic information reduces the candidate population for a specific drug. In the development of pharmacogenomics the following sequence of steps is envisioned. Gene sequencing will lead to the identification of variations in gene sequences, followed by the identification of functionally significant variations and eventually clinically important functionally significant variations in gene sequence. The benefits of pharmacogenomics are expected to be the avoidance of adverse drug reactions and the ability to select patients appropriate to a particular drug.

Brian Athey, PhD, Director, the Michigan Center for Biological Information (MCBI), the University of Michigan spoke on: "The Interface of Information, Imaging, and Genetics". The bioinformatics world is viewed as a grid with three layers: users (scientists and engineers), middleware (bioinformation, security) and clustered operating systems. The issues involved are often in the field of information science rather than computing science; for example, finding information on different databases. The University of Michigan visible-human project was given as an example of a working system. A number of consortiums, involving genomics, structural biology and proteomics are being linked by Michigan's high-speed networks. The Michigan system serves as a demonstration which must now move to adoption.

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