The Pharmacogenomics Journal (2003) 3, 303

www.nature.com/tpj

Pharmacogenomics and clinical medicine: passing flirtation or marriage?

The Pharmacogenomics Journal (2003) **3,** 303. doi:10.1038/sj.tpj.6500214

In the conference 'Hot Topics in Pharmacogenomics,' a joint meeting of the International Society of Pharmacogenomics and the Pacific Rim Association of Clinical Pharmacogenetics (Los Angeles, November 3–4, 2003, http://www.pharmacogenomics.org – full meeting report to follow), there was the presentation of dialectically opposite points of view on the impact of pharmacogenomics in clinical medicine. While Daniel Nebert (University of Cincinnati) stated that pharmacogenomics would not impact on clinical medicine, others such as Urs Meyer (University of Basel), Magnus Ingelman-Sundberg (Karolinska Institute), Richard Weinshilboum (Mayo Clinic), David Flockhart (Indiana University), Ronald Krauss (Lawrence Berkeley National Laboratory), Tamas Bartfai (Scripps Research Institute), and David Goldstein (University College London) were far more optimistic about the potential impact of pharmacogenomics on medical practice.

Why this debate now? Are there any doubts that the enormous progress in genomics will indeed be translated to clinical medicine? What are the roadblocks and the opportunities for this field? In my opinion, there are two aspects to progress in the field. The first, and historically older, is in the pharmacokinetics (PK) arena, and the other is in the area of pharmacodynamics (PD). Progress in the genetic basis of PK pathways has been consistent and genotyping already guides therapies in some instances. For example, thiopurine methyltransferase (TPMT) genotyping is clinically indicated and performed in some types of cancer treatment, thanks to the pioneering work of Weishilboum.[1]

Genetic variations in genes encoding cytochrome *P*450 enzymes, such as CYP2D6 gene deletions and duplications, are also well characterized and it is just a matter of time before genotyping for drug-metabolizing enzymes reaches the clinic.[2]

The challenge for the field is to go beyond PK, and achieve conclusive results on PD-related genes that affect the outcome of pharmacological treatment. While candidate gene approaches may offer some promise, the paucity of strong candidates in many areas (such as psychiatry) makes the search for new targets particularly relevant. In this regard, it may pay off to go beyond the usual candidates and conduct genome-wide searches that may identify novel and unexpected targets. This potential highly powerful approach has been limited by issues of technical feasibility and cost.

This was specifically addressed in the 'Hot Topics in Pharmacogenomics' conference by Francis Collins, Director of the National Human Genome Research Institute, National Institutes of Health, who gave an informative overview of the international haplotype mapping (HapMap) project (http://www.hapmap.org), which is a partnership of scientists and funding agencies from Canada, China, Japan, Nigeria, the United Kingdom, and the United States, to develop a public resource that will help researchers find genes associated with human disease and response to pharmaceuticals. The goal of the International HapMap Project is to develop a haplotype map of the human genome, the HapMap, which will describe the common patterns of human DNA sequence variation. The HapMap is expected to be a key resource for researchers to use to find genes affecting health, disease, and responses to drugs and environmental factors. The information produced by the Project will be made freely available.

It is estimated that the cost of genome-wide genotype based on haplotype markers will be less than 5% of the cost of direct sequencing across the genome. Such a substantial difference in price will make genome-wide screening for complex phenotypes (including the phenotypes of drug response) go from an unreachable goal to a feasible scientific endeavor that will certainly be pursued by research groups worldwide. It is hoped that advances in technology making it possible to search for new targets across the genome will permit the conduction and replication of studies aimed at identifying PD markers of drug response. This type of achievement in various populations would lead to a new scientific foundation for our field, which would facilitate the bridging of the gap between research concepts and clinical medical practice in pharmacogenomics.

REFERENCES

1 Lennard L, Van Loon JA, Lilleyman JS, Weinshilboum RM *Clin Pharmacol Ther* 1987; **41**: 18–25.
2 Ingelman-Sundberg M, Oscarson M, McLellan RA *Trends Pharmacol Sci* 1999; **20**: 342–349.

J Licinio
Center for Pharmacogenomics, UCLA Neuropsychiatric Institute and School of Medicine, Gonda Research Center 3357A, 695 Charles Young Drive So., Los Angeles, CA 90095-1761, USA
E-mail: licinio@ucla.edu