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The Pharmacogenomics Journal

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Welcome to The Pharmacogenomics Journal

What will define medicine in the 21st century? When confronted with the future, my first instinct is to look at the past for hints. Major hallmarks of the 20th century have included the discovery of antibiotics, vaccines, chemotherapy, progress in surgery and anesthesiology, and treatments that if not curative, have brought considerable alleviation to chronic diseases, such as heart disease, diabetes and mental illness. Supporting these clinical achievements, progress in basic science has given us new insights into the molecular basis of disease. Are we poised for the next step in medicine, the utilization of DNA sequences to identify new treatment targets and the introduction of more effective—and personalized—therapies?

History will show the sequencing of the human genome as a defining event of the 21st century. The fact that two groups—an international consortium of publicly funded institutions and a privately run effort—could, despite their structural and cultural differences, successfully come together to the finishing line of sequencing the human genome is a momentous accomplishment. The results of this endeavor provide a new level of opportunity for scientific progress. In this inaugural issue of *The Pharmacogenomics Journal* we have news and commentary on the human genome sequencing effort (see pages 5–12). It is a remarkable achievement to make available to anyone anywhere unprecedented amounts of information containing nothing less than the blueprint of humanity. What will we do with those terabytes of data? How can they be processed? How can such knowledge be diffused efficaciously and affordably? Who will profit from it? Will some people be exploited? Who will be left at the margins of such emerging progress? Who will be propelled forward at its crest? Does it still make sense to think of haves and have-nots? Or will such an avalanche of knowledge eventually filter down to all of us?

I believe that the starting point of the applications of the human genome sequencing effort is in the emerging field of pharmacogenomics, which is the focus of *The Pharmacogenomics Journal*. In this new field the sequencing of the human genome can lead to fundamental advances in science and better treatments that successfully alleviate the suffering of human disease. These possibilities have been highlighted in leading scientific journals and in the popular press.[1–3]

The up-and-coming field of pharmacogenomics brings together clinical pharmacology, genetics, genomics, and proteomics. It is exciting to see an area of knowledge emerge and coalesce before our eyes. We have dedicated our efforts to bring such excitement, promise, and new discoveries to the pages of *The Pharmacogenomics Journal*.

The use of genome-based technology, such as SNP (Single Nucleotide Polymorphism) maps, is promising to transform clinical pharmacology. Information is emerging that will make it possible to quantify and classify scientifically what had been traditionally relegated to the amorphous category of 'individual differences.' We have all known throughout our professional careers and personal lives that different people respond differently to the same treatment. Some can be cured, others do not respond, and a smaller number develop side effects or idiosyncratic reactions, some of which can be fatal. However, in most cases it has not been possible to identify *a priori* how an individual would respond to a drug. The promise of pharmacogenomics is that studies using genome-based technology will lead to the identification of markers that predict both positive and negative responses to drugs. Such advances would bring to market drugs that would be individually tailored for optimal response. In the not-too-distant future what will be surprising is the fact that medications were once prescribed *without* assessment of individual factors that predict clinical responses and levels of drug metabolism.

There are four principal components in the field of pharmacogenomics. The

first is based on the study of polymorphic variations in the genome. This includes discovery of relevant polymorphisms, the study of the biological impact of such polymorphisms, and the association of such polymorphisms to drug response. Several articles in this issue cover those areas. Our review section has an article by Brinkmann and Eichelbaum (pages 59–64) on the important area of polymorphisms in the multidrug resistance gene (*MDR1*) which influence the distribution and bioavailability of P-glycoprotein substrates, such as digoxin. The original research article by Pullarkat *et al* (pages 65–70) shows that polymorphisms of the thymidylate synthase gene may have the potential to identify patients with colorectal cancer who are more likely to respond to fluoropyrimidine chemotherapy. The new data of Serretti and colleagues (pages 71–77) show an association between the short variant of the upstream regulatory region of the serotonin transporter gene and poor response to the prophylactic effects of lithium in mood disorders. The results from Fukushima *et al* (see pages 78–83) show that a polymorphism of the human histamine H2 receptor gene is functionally relevant. The important issue of pharmacogenomics, ethnicity, and susceptibility genes is discussed in the perspective by Nebert and Menon (pages 19–22). The integration of pharmacogenomics to specific clinical entities is the focus of our section *Clinical Implication* (see pages 27–37), which in this issue covers asthma.

The second and equally important area of pharmacogenomics is the identification of the effects of drugs at the genomic level. Progress in this area will lead to the identification of new targets for drug development that may be more specific and with fewer side effects than existing compounds. A crucial component of such effort is the use of relevant animal models. The review article by Gould Rothberg (pages 48–58) discusses expression pharmacogenomics in the context of animal model systems commonly used for pharmacokinetic, pharmacodynamic and toxicologic analyses.

The third major area of pharmacogenomics is the study of drug–genome interactions at the most fundamental level. This will lead to new key discoveries that will expand the frontiers of existing knowledge not only in medicine, pharmacology, and translational research, but also in biology and science. Progress in this area will, with the help of bioinformatics, take us from nucleotide sequence to structure and function. In the article by Bailey *et al* (pages 38–47) current opinion in structural biology is related to recent developments in computational drug design.

The last area of new development is the highly important field of post genomics. As detailed in the elegant perspective by Corthals and Nelson (pages 15–18), the number of coding genes in the human sequence (26 000–31 000) compares with 13 000 for a fly, 18 000 for a worm, and 26 000 for a plant. It is remarkable that the biggest difference between humans, worms, or flies is the complexity of our proteins: more domains (modules) per protein and attendant novel combinations resulting from alternative assemblies of these modules. Proteomics research, particularly expression proteomics—the qualitative and quantitative display of protein expression profiles of tissue extracts or cells—is a key component of the field of pharmacogenomics and will be well represented in this journal.

Such a vast array of science demonstrates that pharmacogenomics is not just a better tool for patient care, therapeutics, and drug development. It represents above all a conceptual revolution and a paradigm shift. It moves pharmacology beyond drug action and leads to the systematic study of drug interactions with a multitude of genomic and proteomic targets, resulting eventually in a much enhanced knowledge basis in biology. As with every new approach there may initially be excessive expectations. A full and realistic assessment of the field, with a balanced account of opportunities and pitfalls, can be found in Klaus Lindpaintner's article on pages 23–26.

The Pharmacogenomics Journal has been developed to be a vehicle for the reporting of progress in the exciting and emerging area of pharmacogenomics. We will publish high-quality original research articles, after timely and rigorous peer-review. Of course progress in pharmacogenomics will have ethical, economic, legal and social (EELS) implications, which have to be thoughtfully explored. The front part of the journal consists of news & commentary, perspectives, an EELS article, clinical implication, correspondence and reviews.

I am very grateful to the editorial board, which includes internationally recognized leaders from academia, industry, and government, whose expertise will ensure a diversity of balanced perspectives. I am also delighted to be working with the team at Nature Publishing Group Specialist Journals, whose insight and dedication have brought the launch of the journal to fruition.

The Pharmacogenomics Journal welcomes new ideas and new areas of investigation. We invite authors to submit their work to the journal (electronic submission will be available shortly) and look forward to receiving exciting new data. All papers that are accepted for publication will have their abstracts published on the web in advance of print. More details can be found at the journal's website (http://www.nature.com/tpj).

One of the most fascinating developments of early 21st century science will be the rapid growth of the field of pharmacogenomics. *The Pharmacogenomics Journal* will be the primary vehicle for the publication of such progress.

DUALITY OF INTEREST

None declared.

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