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Pharmacogenetics to come

Genetically selected medicine has been much hyped but has significant potential. Regulation and treatment will depend on pharmaceutical companies more readily sharing genetic data.

We all know someone who will laugh immoderately at bad jokes after a small glass of champagne, and someone else who can down several pints of beer and yet still discuss celestial mechanics with intellectual clarity. This is happy-hour pharmacogenetics in action.

Clinical pharmacogenetics works on the same principle — that people react individually to different drugs. It is a less light-hearted affair. Every year, hundreds of thousands of deaths worldwide can probably be attributed to the side effects of drugs; and hundreds of thousands of patients will take drugs that for them have no effect at all.

Thanks to new genomic technologies, it is getting easier and cheaper to identify the subtle genetic differences — 'SNPs' (single nucleotide polymorphisms) — that are responsible for such diverse responses (see page 760). Drug-regulatory agencies are now confronted with the problem of how to respond, and the challenge is not an easy one.

The popular, and much-hyped, image of a straightforward glide into perfect, personalized medicine is way off the mark. No one yet knows how predictive SNPs will be in identifying individuals who are likely to suffer side effects, or who may not benefit, from a particular drug. In some cases, when a polymorphism in a single gene dictates potentially lethal side effects in a drug for a serious disease, the benefits clearly outweigh the costs. But in most cases, large numbers of SNPs are likely to be required to profile those who may benefit or suffer — pushing up the cost without necessarily delivering a level of predictive certainty that will put physicians at ease. In treatment of non-life-threatening diseases, who decides when it is no longer worth incurring costs just to derive a slightly increased certainty of efficacy?

Regulatory agencies are now trying to decide what genomic data they should demand from pharmaceutical companies wanting to bring new drugs onto the market. In mid-November, the opinion-setting US Food and Drug Administration (FDA) will hold its second workshop on pharmacogenetics in drug-regulatory decision-making. It aims to define guidelines to encourage drug companies to submit genomic data, reassuring them that FDA staff will not try to make predictions of possible toxicity from raw data that few are as yet used to interpreting. The agency's first meeting, in May last year, exposed the conservatism of many big drug firms. They are afraid of being forced to abandon their traditional blockbuster approach of drug development in favour of the potentially less lucrative method of targeting therapy to restricted groups of patients most likely to benefit. But they are enticed by the possibility of greatly reduced costs for clinical trials.

Conscious of the industry's fears, the FDA wants to avoid disincentives to producing new drugs. And nobody knows how the data will be used. Hence the non-threatening and vague terminology — 'guidelines', 'encouragement', 'reassurance'.

But openness will have to increase. We are starting to learn more about the predictive value of SNPs from academic clinical studies on approved drugs. This information will slowly accrue. As the price of identifying SNPs falls yet further, physicians should expect to receive more pharmacogenetic data from drug companies, along with appropriate genetic tests, to help them select the best therapy for an individual patient. The smartest physicians will use this information appropriately — while not forgetting that a full and accurate description of clinical symptoms and exact diagnosis are equally important in interpreting such data and selecting therapy. Weakness in clinical data collection is universally acknowledged as a serious hindrance to pharmacogenetics.

The pharmacogenetic learning curve is not particularly steep — experience of the principles has been gathering slowly over the past half-century — but it will be long and grinding for all sides. The stakes are high and the future uncertain. There is no doubt that pharmacogenetics will improve therapeutics, but it will arrive gradually, and will not provide a panacea. ■

New access for agriculture

A United Nations scheme launched last week extends unrestricted access to *Nature*'s content within developing countries.

It is gratifying, as staff at *Nature* have found, to meet researchers in infectious diseases in the world's poorer nations and discover that they are making use of their privileged access to our content. Since March 2002, researchers, policy-makers, educators and others in more than 1,000 institutions in 100 or so developing countries have been receiving *Nature* free of charge online as part of the Health InterNetwork Access to Research Initiative (HINARI).

Led by the World Health Organization, this United Nations initiative includes all of the journals published by Nature Publishing Group (NPG), and 2,000 or more from other publishers (for details see www.healthinternetwork.org/src/eligibility.php). Web statistics show that significant and increasing use is being made of this accessibility, for which the HINARI secretariat acts as gatekeeper. It includes all countries whose annual GNP per head is less than US$3,000. (Publishers may charge reduced prices for access in the less impoverished of these countries, but NPG has elected to provide free access for all.)

An equivalent scheme for researchers in agriculture was launched on 14 October by the Food and Agriculture Organization of the United Nations. Inevitably, it has an acronym: AGORA (Access to Global Online Research in Agriculture) — see www.aginternetwork.org/en/about.php. As with HINARI in its first phase, all publishers sign up to providing free access to researchers and others in countries where the GNP is less than $1,000 per capita (there are 69 eligible countries — see www.who.int/library/reference/temp/eligible_countries.pdf).

It is worth adding that *Nature* actively supports another free-access distributor of its content that is targeting the developing world: SciDev.Net (see www.SciDev.Net), financed by foundations and government departments for international development.

We at *Nature* are delighted to contribute to the principal goal of AGORA: to increase the quality and effectiveness of agricultural research and training in low-income countries, and thereby to improve food security. ■