editorial

Kewal K. Jain

A critical review of the Royal Society's report on personalized medicine

The recently issued report, 'Personalized medicines: hopes and realities' by the Royal Society, UK, has identified important areas of application and the problems facing development of personalized medicine [1]. It is an excellent review of the topic, pointing out the advances, as well as limitations, of personalized medicine. Some important conclusions were:

- The report predicted that pharmacogenetics is likely to become increasingly important in drug discovery and development as genetic factors help to identify optimal patient populations to be treated by a particular drug.
- The report also suggested that information is needed about the use of pharmacogenetic screening for existing medicines, including generics.
- The report recommended regulatory oversight of postmarket monitoring beyond Phase III clinical trials, exploring links between genetic variability and clinical outcomes where this is considered to be important.

Limitations identified by the report include a shortage of scientists who are trained in the appropriate areas of personalized medicine (required for further research). The report identified the need to improve the education of medical students and physicians working in the field of personalized medicine.

Recommendations in the conclusion of the report are worthy of consideration by decision makers in healthcare. However, the following conclusion of the report is subject to debate: 'its true potential may not become apparent for 15–20 years, during which time a great deal more information may become available about the practicalities of applying information derived from complex multifactorial systems in the clinic.' Here, 15–20 years is concluded to be the minimum period of time required to gain an understanding of the patient's genetic make-up – well enough so that it becomes a major factor in determining which drugs are prescribed. This length of time is considered to be an overestimation if one takes a broader overview of personalized medicine and the progress made during the past decade. Considerable knowledge on pharmacogenetics has accumulated during the past several decades. The problem is not so much the lack of knowledge but its translation into medical practice. The tools are becoming available and knowing the complete genetic make-up of an individual is not a prerequisite for improving the medical management, and might not be required in all cases for safety and efficacy. The process of educating the physician has started and should not require 15–20 years for the current generation of doctors. If we tell older physicians that personalized medicine will not be a reality for another 15–20 years they will not consider it, because they would be retired by that time and might not bother to use the knowledge, which is already available, to improve patient care.

Multiple technologies relevant to personalized medicine

The word 'medicines' in the title of the report refers to personalized drugs, unlike the word 'medicine' in 'personalized medicine',

1359-6446/06/$ - see front matter doi:10.1016/j.drudis.2006.05.005

which indicates the whole concept. Medicines alone do not make up the healthcare system. The report limits its scope to the discussion of pharmacogenetics and pharmacogenomics and does not discuss the role of other technologies (such as pharmacoproteomics, metabolomics, RNA interference, innovative cell and gene therapies, and nanobiotechnology) in the development of personalized medicine. Patients' own cells or tumor cells have been used in cell and gene therapies for some years now. Autologous adult stem cells can form the basis of personalized medicine and do not require pharmacogenomics or pharmacogenetics. Drug actions do not always correspond to genotyping and personalized gene therapies were in development before the sequencing of the human genome was completed. Many environmental and other factors, besides genetic factors, determine adverse reactions to drugs. Drug safety has made considerable advances in the past decade. Knowledge of pharmacogenetics is enabling the prescription of safer forms, and combinations, of drugs, as well as helping to avoid drug use in patients who are likely to have adverse reactions to them. Translating the existing knowledge during the next five years will reduce the adverse drug reaction problem considerably. Complete knowledge of the genetic make-up of an individual might not completely eliminate the problem of adverse drug reactions, even in 15–20 years.

Compared with other biotechnologies the scope of personalized medicine is much wider, and molecular diagnostics occupies a central stage. In the past five years, rapid advances in genomics, proteomics, metabolomics and nanotechnologies have refined molecular diagnostics with applications in drug development, integrated healthcare (genetic screening, prevention, early diagnosis, monitoring of therapy, etc.) and personalized medicine.

If one reviews the progress during the past decade, current developments in molecular diagnostics have surpassed the forecasts. Molecular diagnostics that are already on the market (e.g. AmpliChip™ CYP450 [2]), and other technologies that will be available in the next five years, will fulfill many of the needs of personalized medicine. Personalized medicine is already a reality in diagnostics. Rapid advances are taking place in other related technologies. Quantum dots, besides refining cancer diagnostics, could also serve as targeted therapeutic anticancer agents [3]. This integration of diagnostics and therapeutics is a form of personalized medicine.

Development of personalized medicine in the USA

The report is mostly based on the opinion of experts in the UK and two individuals from North America, but does not include reference to US institutions involved in personalized medicine. Considering that most of the development in personalized medicine has so far taken place in the USA, the Royal Society should have considered more representation of opinion from the USA.

Some US clinics already practice personalized medicine in selected therapeutic areas. Several anticancer drugs are already linked to diagnostic tests – to achieve appropriate patient matches. One disease in which pharmacogenetics is already being applied is acute lymphoblastic leukemia (ALL). ALL is treated with a cocktail of chemotherapeutic agents that include 6-mercaptopurine, 6-thioguanine and azathiopurine. These drugs are broken down by thiopurine methyl transferase (TPMT). People lacking functional TPMT can suffer severe toxicity or death, but these patients can be treated with doses that are much lower than the standard regimen. Physicians at St. Jude's Children's Hospital (Memphis, TN, USA) and at the Mayo Clinic (Rochester, MN, USA) are prescreening patients to determine if they have functional or non-functional TPMT. The dosage of the components in the chemotherapeutic cocktail is then tailored precisely to the patient's molecular make-up – personalized prescribing.

Role of the biopharmaceutical industry

The traditional focus of the major pharmaceutical companies was on the development of 'blockbusters'. The research and development focus of the pharmaceutical companies is now undergoing a change and the development of personalized medicines is considered to be a valid proposition in an atmosphere where there is still a shortage of promising new drugs in development. The pharmaceutical industry has now taken the major initiative in the development of personalized medicine but the technologies are developed by small biotech companies that do not have the resources to develop the practical applications. Collaborations between biotechnology and pharmaceutical companies, which have been increasing during the past five years, are facilitating the development of personalized medicine. An example of this is the development of AmpliChip™ CYP450 by collaboration between Roche and Affymetrix. Molecular diagnostic companies provide pharmacogenomic tests for clinical trials, which are conducted by pharmaceutical companies. Pharmacogenetics and genomic developments started in the academic environments. Most of the recent progress relevant to personalized medicine development has taken place in the pharmaceutical sector, and has not been published nor has it completed the approval process. No assessment of personalized medicine can be complete without an overview of research and development in the industrial sector. A survey has been carried out continuously since 1997, when only a handful of companies were involved in this area, and published, along with monthly updates that currently include activities of 185 companies (10 major pharmaceutical and 175 biotech) [4]. The few companies listed in the Royal Society report are not representative of the commercial sector – even in the UK.

Concluding remarks

The progress in the field of personalized medicine and related technologies justifies a more optimistic view than that depicted in the Royal Society report. The concept of personalized medicine is becoming accepted by the medical profession, the FDA, health insurance organizations and the biopharmaceutical industry. There are certainly challenges facing personalized medicine but several of the ethical, social and economic factors are already being addressed. We do not have to wait 15–20 years to see the potential of personalized medicine in practice. Moreover, not all diseases will need a personalized approach to therapy (or a combination of diagnostics with therapeutics). Application of new technologies and medicines depends on the personal judgment and decision of the treating physician in each case. Personalized approaches are used by informed physicians and their use is expected to increase. There will be significant personalized medicine activity in the

clinical (as well as biopharmaceutical) sectors in the USA by 2010 and in the UK by 2015.

Perhaps the conclusions and findings by the Royal Society are meant for the National Health Service in the UK alone, but the estimation of the time it will take to introduce personalized medicine is still too long. After the USA the UK is considered to be the country with the most favorable healthcare and scientific environment for the development of personalized medicine. Readers throughout the world watch scientific developments in this area in the UK with great interest. This justifies critical comments on the report issued by a prestigious UK body that has international scientific impact.

Conflict of interest

Jain PharmaBiotech promotes the development of personalized medicine, but does not have any products or financial interests in this area. Professor Jain publishes and lectures on the topic of personalized medicine. The activities are not supported by any government or commercial grants.

References

1 Anonymous, (2005) *Personalized medicines: hopes and realities*. The Royal Society, London, UK
2 Jain, K.K. (2005) Applications of AmpliChip CYP450. *Mol. Diagn.* 9, 119–127
3 Jain, K.K. (2005) Role of nanobiotechnology in developing personalized medicine for cancer. *Technol. Cancer Res. Treat.* 4, 645–650
4 Jain, K.K. (2006) *Personalized medicine: technical and commercial aspects*. Jain PharmaBiotech Publications, Basel (regularly updated since original publication by Decision Resources, Waltham, Massachusetts in March 1998)

Kewal K. Jain
CEO, Jain PharmaBiotech,
Bläsiring 7, CH-4057 Basel,
Switzerland
email: jain@pharmabiotech.ch