Responsibilities in the post genome era: are we prepared?

S Kumar Singh

The successful completion of the human genome sequence can be counted as one of the most important scientific achievements in biology in recent times. The analysis of the draft sequence by two groups, the human genome consortium and a private company (1,2), has revealed astonishing insights into the genetic blueprint of the human race. It has also provided tantalising clues as to what makes us a unique species.

To cite a few examples, the analysis of the draft human genome sequence has revealed that (a) humans have a total of only about 31,000-39,000 genes which is only fractionally higher than the 18,000 genes of Caenorhabditis elegans — a worm — and 26,000 genes in Arabidopsis- a plant (compare these with 6,000 genes in yeast and 13,000 in Drosophila - a fly). (b) Less than 1.1-1.4% of the 3.2 billion basepairs codes for a functional gene products while the rest 98% are mostly repetitive DNA with an as yet unidentified function. (c) About 50 % of the genome consists of the four classes of repetitive DNA segments, many of them interspersed as large islands throughout the genome. (d) There are vast stretches of DNA deserts devoid of any genes at all on certain chromosomes, while there are dense gene clusters on others. (e) More than 1.42 million single nucleotide polymorphisms (SNP, these indicate the degree of variability of an allele in a population) have been identified in the draft version of the genome with many more likely to be identified in the near future. These polymorphisms are likely to be the hotspots of genetic variations and the probable cause of various genetic pathologies and hence are likely to be the first search targets by medical researchers.

Much of this knowledge was unheard of even a year ago. New, mind-boggling facts are being unravelled about our genetic make-up almost every day. New results and hypotheses on human genetics are being proposed, tested and in some cases disproved (3). New technologies are demonstrating their potential to unravel useful medical information from the genetic data.

The first glance at the raw sequence data has yielded important insights on phenomena like addiction (4). Numerous key protein targets have been identified for targeting by immunomodulatory treatments (5) and more than 10,000 of disease causing genes in humans and their causal mutation have been catalogued (6, 7).

It is clear that even by conservative estimates, the impact of this research on any field of human biology — especially medicine — is likely to be staggering. While there may be little in terms of immediate benefit to the general medical practitioner (especially in India), there is much cause for optimism as the genome sequence is likely to provide a fertile hunting ground for medical researchers to probe the molecular underpinnings of many diseases. This is evident from the unprecedented increase (in the developed world) in investment of manpower and financial resources in both academia and commercial ventures in research projects that exploit the new information. Many suspected cases of rare medical anomalies go unnoticed during routine investigations in Indian hospitals. Cheap and rapid screening methods that are likely to emerge in the near future could enable the 'doctor on the street' to quickly screen the average patient with little investment in cost and manpower.

There is however a darker side to this story. Led by the prospects of untold riches and the urge to gain biotechnological leadership, there has been a scramble among commercial ventures to patent DNA sequences which are suspected to be involved in critical disease processes and thus have potential commercial value. The rapidity with which this field has advanced has given little time for legislatures to formulate laws on complex genome related legal and ethical issues.

The Indian contribution to the genome endeavour has been dismal from the beginning, almost non-existent. Like in most cases, Indian science has adopted the wait-and-see approach even as the genomic gold mine lies bare in front of us with all its prospects. Today India with its diverse population base distributed over a vast geographical area is uniquely placed to gain from these evolving technologies. The multicultural and multiracial nature of our society has a rich and diverse genetic resource inherently embedded in it.

One of the main reasons for the success of this project was the tremendous advancement made in various technologies like automated sequencing methods, increase in computational power and advanced algorithms for sequence assembly and annotation. Many of these techniques were unthinkable even five to six years ago. It is clear that if India is to benefit from these technologies and realise the full potential of its vast genetic resources, there must be a paradigm shift in the manner in which basic and applied research is practised, be it in isolated labs or large collaborative studies.

Biomedical and genomic technologies existing today can tinker with the genetic makeup of reproductive cells. This can have profound consequences on and affect lives of millions of people at a fundamental level. Will this knowledge be used to benefit us in hitherto unforeseen ways? Or will it unleash new ghosts from the Pandora's box? These are questions for the future. Nonetheless, it is clear that new ethical and moral questions are likely to be hotly debated in scientific circles.

The need of the hour is to create awareness, among biomedical research personnel and practitioners, of the new opportunities — and the dangers – in emerging technologies. There should be a concerted effort among the academic scientific community and medical

S. Kumar Singh, *Ph.D, Post-doctoral research scientist, Dept of Biochemistry, University of Texas Southwestern Medical Center, Harry Hines Blvd, Dallas TX 75206 USA. Email: skumar@biochem.swmed.edu*

practitioners to rapidly (albeit cautiously) apply the new technologies to problems of immediate national concern. This has to be correlated by an appropriate increase in funds available for projects which focus on the use of these methodologies for problems relevant in the Indian context. The decision of the department of biotechnology, to fund areas in stem-cell research on cataract and the brain is a step in the right direction. The impressive strides made by indigenous academic research centres and commercial laboratories in stem cell research are indeed commendable.

Regulatory bodies which monitor the ethical practices of medical personnel, and those monitoring the preservation of indigenous genetic material, will have additional responsibilities. They must set up ethical and regulatory standards on experimental protocols so that the interests of subjects are safeguarded. Ethical and responsible conduct is going to be increasingly necessary in light of the power of the emerging technologies (8).

This will go a long way in restricting the 'drain' of the nation's valuable genetic resources while exploiting the full potential of local resources, with which India is richly endowed.

References:

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"Doctors, who for the sake of monetary gain do tests for sex determination and pre-conception sex separation and resort to selective female foeticide, are a terrible blot on the medical profession and the government should take the strongest possible action to penalise such people. They might have acquired degrees and become literate but unfortunately cannot be called educated, for literacy without education is like a body without a soul."

Dr Neerajana Sosi, Mumbai, in a letter to *The Times of India*, December 8, 2001.

FMES activities: some highlights

The General Body Meeting of the Forum for Medical Ethics Society was held on September 2, 2001. *Some of the subjects discussed were: our subscription base, themes for future issues, and other projects for the organisation. We need to do a systematic analysis of who subscribes to IME, who renews and who doesn't. Our current strategy for increasing subscription includes a small number of complimentary subscriptions in the hope that they will eventually subscribe. We also depend on the enthusiasm of our members.* ***Some themes for future issues****: medical ethics in general practice; violence by, and against, doctors; the cut practice: a debate; medical records; the influence of managed care, and guidelines for interaction between the pharmaceutical and medical supplies industries and the medical profession.* ***Among future projects*** *are: organising meetings with our contacts, and an anthology of the last nine years of the journal. We also hope to have regular quarterly meetings for discussions on current issues relating to medical ethics.*

Discussion on the proposed Maharashtra Clinical Establishments Act was held on October 28, 2001. *The discussion included both members of the FMES and others concerned with the subject. The MCEA is a proposed revision to the Bombay Nursing Homes Registration Act. Current revisions are the consequence of an earlier campaign in relation to a case of medical negligence in a private hospital. FMES was one of the organisations represented at a workshop on the MCEA, organised on behalf of the Maharashtra Health Systems Project. The MCEA is considered important because it will affect all aspects of medical practice. One question is: will it be an effective tool to make the private sector more accountable?*

Future plans: *In September, we also held two workshops, which were mentioned in the last activities report. The April 2002 issue should carry these workshop reports in more detail. FMES is regularly being approached to organise such workshops, on various aspects of medical ethics. The next one, in collaboration with the Kerala Health Studies and Research Centre in Trivandrum, will be on research ethics, to be held in late January 2002.*

The last few months have also been a time for laying down the foundation for future work. It is becoming clear that the organisation will need funds in order to grow further, whether in terms of IME's subscription base, or the quality of the journal, or other activities such as bringing out other publications, reaching out to a larger readership, developing our site and interacting with the medical/health community within India, as well as in elsewhere in the world. In the last two months, we have made tentative steps for such fund-raising, and will report in more detail as these progress. We also hope to carry a discussion on plans for the organisation, and funding these plan, in a future issue of the journal.