The Human Genome Sequence: a dilemma or an opportunity?

Many fears were expressed in the media when the first reproductive human cloning was announced. While this has sparked off informed debate in the western scientific community, in India, both the medical and the scientific community at large appear to be unconcerned. However, we must be ready for paradigm shifts in the health-care system following from the insights into DNA sequences of human and other life forms, and the associated technologies that will emerge.

Technical questions

From the discovery of genetic basis of diseases by Archibald Garrod in 1901, the sequencing of the human genome, 3 billion long string with the resolution of a single base (A,T,G and C), is a great stride in human history (1). The questions that this raises will be addressed by each country based on its perceived needs and resources. Are we prepared to accept the consequent challenges?

Since the dawn of human society, we have tampered with the genetic make-up of livestock and crops to select useful traits. A century ago Mendel's generalised rules governing the mechanism of inheritance gave birth to the science of genetics. Eventually, in medicine the application of this knowledge ushered in a scientific approach to disease diagnostics and family counseling, a therapeutics revolution with antibiotics both natural and synthetic, and finally, following the advances in recombinant DNA technology, genetically engineered drugs and diagnostics. These occurred gradually in nearly distinct steps of sophistication spread over the entire 20th century.

The Human Genome Project was justified largely on the basis of its medical benefits (2). How is this knowledge going to be useful to us as a developing nation? Will technologies emerge towards more effective and economical health-care practices? Can this knowledge substitute for current medical care practices? Where should we focus our limited funds for R & D to optimally use this knowledge? Can we become equal partners in contributing to and utilising global technological developments of an altogether new type and sophistication? The medical profession must give serious thought to such questions.

This knowledge will allow the prenatal and pre-symptomatic diagnosis of disease genes and predict an individual's occupational risks. The sequence of individual genes on structural analysis mostly in silico will tell us how they function and are regulated, to help us understand biological processes. The sequence data and analysis will provide the framework for new drug design and therapies including gene therapy in some cases. Mapping populations with microchip technology will allow us to conduct mutation screening susceptibility to diseases. This knowledge could dramatically change our approach to health care. Indeed, the Human Genome Diversity Project will study DNA sequence data from varied populations globally, and map diseases like thalassaemia, diabetes and sickle cell anaemia to determine if these are due to random changes in the gene pool or to adaptation to local conditions (3). However, only a few diseases originating from a single gene defect will be amenable to gene therapy in the foreseeable future. Most are multi-genic and multi-factorial, and their complexity will not yield easily with current technologies in spite of genome sequence data of the highest accuracy (4).

The ethical dimension

Prenatal and pre-symptomatic diagnosis of disease provokes many ethical concerns. In addition, many will oppose human cloning. The use of embryonic or stem cells, whether normal or genetically altered, for medical use or research, will be an area of dispute. Researchers will disagree on how far these can genetically tampered without crossing ethical limits. More importantly, they will have to agree on a definition of consciousness and demarcate the stage of growth up to which an human tissue could be used for commercial and medical purposes. Without an informed debate on these issues, we may not benefit from post-genomic technological advances in our country.

A real danger

In India, scientific activity has little impact on the growth and dissemination of knowledge. Students are taught to memorise facts instead of developing their analytical abilities. This served commercial interests; pharmaceutical companies influence prescribing practices by feeding doctors easily digestible 'capsules' on their products. The poor quality of genetics in medical education will keep our doctors captives of marketing forces.

In recent history we have regressed to a state when the scholars managing our universities forced in astrology as a formal subject. As the genome sequence sets new trends in drug design and disease management, requiring analytical skills and creativity comparable to that in developed countries, Indian doctors could enter a similar phase of obscurantism if our education is not immediately overhauled.

Doctors and teachers in India face an uphill task in the new world. With our infrastructure in IT and globalisation of basic knowledge base, now indeed is their opportunity to re-establish the high ideals of their professions both in research and service.

Suggested reading

1. The human genome. *Nature* 2001; 409: 745-964.

2. Strachen Tom and. Read Andrew P. *The Human Genetics*. BIOS Scientific Publisher, 1996

3. Kline R M : Whose blood is it, any way? *Scientific American* 2001; 248: 42-49.

4. Chapella A de La : The land between Mendelian and Multifactorial Inheritance. *Science* 2001; 293, 2213-2214

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