Sequencing the Human Genome: Blessing or Curse?

Ania Kowalski

On April 25, 2003, the entire sequence of human DNA (the genome) was worked out under the Human Genome Project (HGP), a modern scientific milestone [1]. Yet the completion of this project has only marked out paths for the next phase of human biology and genetics, where the focus will move from studying genetics on a population level to individual organisms. The HGP will impact on three main areas: scientific research, medicine and genetic engineering.

The international project to sequence the genome began in 1990, and in 2003, 99% of the genome was elucidated to 99.999% accuracy [1].

Once a sequence had been assembled, the HGP aimed to distribute the information into the public domain within 24 hours. Another important goal was to study the ethical, legal and social implications of genetic research, and 5% of funds were apportioned to the Ethical, Legal and Social Implications (ELSI) Programme. The ELSI Programme researched racial, ethnic and socioeconomic impacts of the HGP [2]. It promoted public understanding of these implications by producing numerous reports and the programme also funded seminars and radio and television programmes in an effort to educate different sectors of society such as policymakers and the public [3].

The HGP developed many new sequencing techniques, which are driving down the cost of sequencing individual genomes. The HGP cost US$2.7 billion [4]. Knome, an American personal genomics company, is currently sequencing the genomes of two private clients at a price in excess of $350,000 per client, a process initiated in January 2008 [5]. These people are expected to be the first to have their genomes sequenced by a commercial company [6]. The overall aim of such companies is to lower the price of sequencing a human genome to $1000. With technological advances, it is likely that sequencing personal genomes will become a feasible medical procedure [7].

The HGP built on techniques developed from sequencing non-human genomes, such as the common fruit fly [8]; the techniques used in sequencing the human genome will in turn be applied to other organisms, with potential benefits to humans. The Microbial Genome Programme builds on the HGP and aims to characterise microbes [9]. It is hoped that this will lead to insight into energy-related biotechnologies. For example, microbes that can readily metabolise waste material and microbial enzymes that could be used in place of toxic chemicals might be key to a cleaner environment [10]. The HGP also demonstrated the power of international collaboration and has paved the way for future research such as the recently proposed 1000 Genomes Project. This is an international collaboration to sequence 1000 humans in order to catalogue genetic variation [11].

Resources from the HGP have the potential to revolutionise medicine. Once disease genes are identified, diagnosing genetic diseases might become routine. Pre-natal tests for diseases that can be managed with medical intervention might become widespread. Phenylketonuria is one such disease - a metabolic disorder that can be treated with an appropriate diet and is already screened for universally in the UK [12]. Some scientists, however, worry about where this could lead: we might eliminate embryos with cystic fibrosis, but if we extend this to late onset diseases [13]; where do we stop?

Another great benefit of the HGP is the full catalogue of genes that provide an alternative approach to therapies. The accuracy and completeness of the catalogue allow systematic searches for the causes of disease: a recent study by the Wellcome Trust Case Control Consortium (WTCCC) identified several genetic regions that increase the risk of developing type 1 diabetes and a region on chromosome 9 associated with coronary heart disease [14]. In the future, such information could form the basis of gene therapy.

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With the sequencing of individual genomes, small regions

of DNA that vary among humans (called polymorphisms) could be used to predict a person's response to certain drugs and allow tailoring of medication to individual patients [15]. More specific medical intervention would help eliminate unwanted side effects [16].

The ethical and legal considerations raised by the HGP can be broadly grouped into categories of genetic information and genetic engineering. The vast cache of genetic information about polymorphisms between individuals has potential disturbing social consequences. Employers and insurers could demand genomic sequences from individuals [17]. Employers might use this information to select employees based on how well they would be suited to a specific job, while insurance companies could discriminate against those at higher risk of certain illnesses. In the UK, a moratorium until 2014 obliges insurance companies not to take genetic information into account when providing life insurance up to £500,000 [18]. An argument against the ban is that genetic information

is already being used to some extent, and using the entire genome would provide a more accurate picture. Currently, companies are allowed the exception of Huntington's chorea, which is a fatal genetic disease [19] and the SRY gene, which confers maleness. However, without the ban, there is a risk of unfair increased premiums or a rejection of insurance if disclosure of genetic tests is granted. A positive test does not make developing the disease a certainty [16].

> **"Resources from the HGP have the potential to revolutionise medicine"**

Genetic predisposition assessed from a genomic sequence is powerful, but environmental and lifestyle factors also affect health. Often, genetic screening of a disease can only determine a probability of developing it, not a certainty. Knowledge, therefore, might come at the price of 'genetic hypochondria' [20], whereby people spend their lives waiting for a disease that might never arrive.

The human genome provides information that will enable scientists to determine the genetic basis of physical and psychological traits, which genetic engineering might be capable of enhancing in the future. The engineering of reproductive cells, affecting future generations, is a contentious issue. Apart from the obvious ethical issue of interfering with natural life processes ("playing God"), there is a danger that certain trends might change over time, such as desirability of emotional or cognitive traits or even tallness, and we might end up following superficial fashions.

The HGP is the beginning of a new era of research into the genetic information we possess. It can be seen as both a blessing and a curse: the potential advances in medicine, which might indeed prove a blessing, must be balanced with the potentially complex and problematic social challenges around the use of, and access to, our genetic information. ■

Ania Kowalski is a second year studying Biological Natural Sciences at Queens' College.

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