

INTRODUCTION

MORAL RESPONSIBILITY AND THE HUMAN GENOME PROJECT

The Human Genome Project (HGP) is now almost completed. A draft of the full DNA sequence of the human genome has recently been published (Int. Hum. Gen. Seq. Cons., 2001; Venter et al., 2001). The project started in 1990 and was planned to be completed fifteen years later. It is now clearly ahead of schedule. But even when the project is completed much work remains—the analysis of the function of the 30-40,000 genes in the human genome is beyond the scope of the project and will last for decades.

However, even before the HGP started, it was rather controversial from an ethical point of view; not so much because of the sequencing work as such, but because of its anticipated consequences. The results of the project might be used, for example, in developing genetic tests, genetically tailor-made drugs, and gene therapies. Some people fear that genetic testing may lead to discrimination in insurance and at the workplace. Some view the pharmaceutical companies' research on genetically tailor-made drugs as an unacceptable commercialization of science. Some anticipate that the development of gene therapy will give rise to a society in which parents want to design perfect babies with genetic enhancement techniques. This forces us to ask: should the HGP perhaps never have been initiated in the first place? Or more importantly: how should the implications be handled now when the project is almost completed?

Some of the ethical issues were anticipated at the planning stage of the project. Therefore, right from the start the funding agencies allocated a certain percentage to ELSI (Ethical, Legal and Social Implications) research. Some people view this as a way for the scientific community to take moral responsibility for the HGP and its consequences. Critics maintain that ELSI research is intended merely to gain acceptance of risky technologies, as a way of making the research legitimate.

This dispute raises the more general question of moral responsibility in human genetics research. What does moral responsibility really mean in this kind of research? What moral responsibility lies with the geneticists as individuals and as a community for the choice of topic, experimental work, publication, and application? Responsibility is not just a matter of blame or praise. First and foremost, it is a normative issue: What can reasonably be the moral obligations of scientists doing this kind of research? What moral responsibility lies with the geneticists for its consequences? Do geneticists have a responsibility for trying to affect other people's applications of their findings?

One might think that such questions about moral responsibility have been discussed a great deal. This is, however, not the case. To be sure, the rhetoric of 'scientific responsibility' is prominent in the debate on the research ethics of genetics, but its meaning is very seldom clarified. In the ELSI research, it is commonly the actual and possible consequences as such that have been analyzed and discussed. The issue of the moral responsibility of the geneticists for these consequences has been very much neglected. It is, however, the key issue of this book.

HUMAN GENETICS AND THE ROLE OF HGP

The Human Genome Project has already been and will in the future continue to be of key importance in many different branches of human genetics research including medical genetics, clinical genetics, pharmacogenomics, and gene therapy research. It is an international endeavor coordinated by the Human Genome Organisation (HUGO), founded in 1988. The coordination concerns the laboratory work itself as well as the administration of the rapidly growing amount of information about the genomes of humans and model organisms (McKusick, 1989; Br. Med. Assoc., 1998, pp. 193-194).¹

The overall objective of the HGP is to map and sequence the human genome. More precisely, the HGP is a project designed to construct genetic and physical maps of the human genome, to determine the complete nucleotide sequence of the human DNA, to localize the genes of the human genome, and to conduct similar analyses on the genomes of some other organisms used as models. Examples of such model organisms are the roundworm *C. Elegans*, yeast, the bacterium *E. coli.*, the mouse, and the fruit fly (NCHGR, 1991; NHGRI, 1997).²

The HGP aims at understanding the structure of the human genes. The understanding of the function of the genes is beyond the scope of the project in the strict sense. But, of course, alongside the mapping and the sequencing, analyses of the function of genes have already started and will continue for a long time after the project is completed (NHGRI, 1997, pp. 61-67). The best way to understand what the HGP is all about is to view it as a kind of tool-making (NCHGR, 1991; Kingsbury, 1997). With the help of the maps and the knowledge of the sequence of the human genome, many other kinds of human genetics research, such as function analysis, genetic drug research, and gene therapy research, can be carried out with precision.

It is important to note that the more specific objectives of human genome research may vary among different countries. In a sense it might be more appropriate to talk about many different human genome projects than a single one.

¹ See also URL: www.gene.ucl.ac.uk/hugo/.

² See also URL: www.nhgri.nih.gov:80/HGP/ and URL: www.er.doe.gov/production/ober/hug_top.html.

From the point of view of HUGO, however, one may speak about one international project (Cook-Deegan, 1994, pp. 187-230).³ It is also important to note that the HGP in the narrow sense is publicly funded, or—in some countries—funded by grants from foundations like the Wellcome Trust. However, there are also very important commercial counterparts, not least the sequencing project carried out by Celera Genomics with J. Craig Venter as principal scientist (Venter et al., 2001).⁴

The most extensive mapping and sequencing efforts are made in the US. In much of the literature about the HGP it is the US project that is explicitly referred to, not the international one. The main agencies responsible for planning and developing the project in this country were the Department of Energy (DOE) and the National Institutes of Health (NIH). The planning process led to the publication of a joint research plan in October 1990, signifying the start of the US project (Cook-Deegan, 1994, pp. 161-185).⁵

If we turn to Europe, it is apparent that by the end of the 1980s only a few teams were mapping and sequencing the human genome. Most of the work was general genetics research, including studies of the function of genes and studies of nonhuman genomes. However, in 1990 the research program Human Genome Analysis was formally announced by the European Community Council of Ministers. The effort was concentrated on specific diseases and particularly interesting areas in the human genome (Hallen, Klepsch, 1995). This can also be seen in the BIOMED programs replacing the original Human Genome Analysis program (Hallen, 1998).

In the literature on the HGP there are numerous references to 'the' human genome. This signifies the 'basic' human genome, i.e., the standard genetic information contained in a typical composite of the 'normal' human chromosomes. This 'basic' human genome is an abstraction that can be compared to the human skeleton. However, it should be noted that there is no ideal example of the genome. In fact, much of the interest in human genome research has to do with variations among individual humans. The HGP is often justified by reference to the identification of disease genes, i.e., genes that deviate from the 'standard' genome.

There are other kinds of human genome research beside the HGP. One is function analysis, which has already started but will continue for many decades after the project in the strict sense is completed. Another kind is 'population genomics', for instance within the Human Genome Diversity Project (HGDP). The aim of this kind of research is to collect and analyze genetic information from ethnic groups around the world.⁶

³ See also URL: www.gene.ucl.ac.uk/hugo/.

⁴ See also URL: www.celera.com, and URL: www.incyte.com.

⁵ See also URL: www.nhgri.nih.gov:80/HGP/ and URL: www.er.doe.gov/production/ober/hug_top.html.

⁶ See URL: www.stanford.edu/group/morrinst/hgdp/summary93.html. See also British Medical Association, 1998, pp. 195.

The tools made available by the HGP, however, are used not only in function analysis and population genomics, but also in clinical genetics, pharmacogenomics and gene therapy research. Such research was, of course, to a varying extent carried out even before any useful results emerged from the Human Genome Project. It is obvious, however, that the genetic knowledge provided by the HGP gives it much better tools. It is therefore reasonable to view such research as applications of the knowledge gained through the project. Another reason for this is that in applications for funding of human genome research these kinds of applications are often referred to as expected beneficial outcomes of the research.

ETHICAL IMPLICATIONS

Human genetics research has important ethical implications for many different agents and parties such as individual patients and their families, different social and ethnic groups, doctors and genetic counselors, public and private health care, biotechnological companies, insurance companies, employers, the government, the general public, and, of course, the geneticists themselves. In this study, I shall focus primarily on the moral responsibility of the geneticists. The reason for this is, as I have stressed above, that this aspect is very seldom reflected on in the ELSI literature. The possible use and abuse of the applications in society and health care have been discussed much more thoroughly.

The Moral Responsibility of the Geneticists

What responsibility do the geneticists have for their choice of subject (topic), the research process in the narrow sense (empirical and theoretical work), the publication of the results, and the application of these results? As the subtitle of the book indicates, I focus in particular on the responsibility of geneticists for the consequences of their research. With regard to these consequences, it is sometimes useful to make a distinction between those that are direct and those that are indirect. The distinction, however, is not strict. The direct consequences of research are those appearing in the research process in itself, for example, the consequences for human subjects participating in a study. The indirect consequences are those of the results of the research after publication, for example, the application of genetic knowledge in other kinds of research or in society. However, what counts as direct and indirect consequences depends on exactly what kind of genetics research we are talking about. For instance, the consequences for human subjects participating in gene therapy research are direct consequences of this research, while the gene therapy research itself, at least to some extent, can be viewed as an indirect consequence of genome research, since it uses knowledge gained in genome research.

Moreover, it is sometimes essential to make a distinction between the responsibility of geneticists as individuals and as a community, between the

responsibility of geneticists in the beginning of their scientific career and those high in the academic hierarchy, and between the responsibility of geneticists working at universities and those working in biotechnological companies. One very important aspect concerns professional policy. What policy should the genetics community have on, for instance, the treatment of human subjects or the applications of genetic knowledge in society? It should be noted that the professional policy of the genetics community is not necessarily identical to the public policy of the government.

This study is in two respects wider in scope than is common in the ELSI literature. As a background to my discussion of the ethical implications of human genetics research, I will devote the first two chapters to more general issues. In Chapter One, I shall discuss the concept of moral responsibility in general. I shall also propose a new ethical framework based on certain empirical findings of the relatively new scientific field called cognitive semantics. Cognitive semantics stresses the metaphorical character of key human concepts. This ethical framework sheds light on the discussion of the ethical implications of human genetics research. It helps us to understand what ethical dispute is all about in this context, and provides a starting point for normative suggestions. In the second chapter, I shall discuss research ethics. Here I shall focus on the concept of moral responsibility of scientists in general. This will put the moral responsibility of the geneticists into a broader perspective. What do we mean by 'moral responsibility' in this specific context? For what are geneticists responsible? To whom are they responsible? Are there any differences in the moral responsibility of scientists doing human genetics research compared to the responsibility of other scientists?

In discussing the moral responsibility of geneticists, it is important to make a distinction between internal and external perspectives. Internal perspectives are the perspectives of the geneticists themselves. External perspectives are those of other people such as philosophers, bioethicists, sociologists, journalists, politicians, the general public, etc. Both kinds of perspectives are legitimate. The internal perspectives are legitimate because it is the geneticists who are carrying out the research. Certainly, they are entitled to make moral judgments on their own work. The external perspectives are legitimate because human genetics research is a social activity influencing the remainder of society in various ways, because it uses the societal infrastructure, and because it is to a large extent funded by taxes. Both kinds of perspectives are also necessary in order to work out well-considered ethical guidelines and policies. Each kind has its advantages as well as disadvantages. The geneticists run the risk of becoming 'home blind' and only seeing their own side of things. People with external perspectives might have a broader societal perspective. A disadvantage of the external perspectives, however, is limited knowledge of scientific facts and limited experience of scientific practice. Deep knowledge and first-hand experience is, on the other hand, the advantage of the internal perspectives. Dialogue is the best way of handling this situation. In this study, I shall discuss the moral responsibility of scientists conducting human genetics research but

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