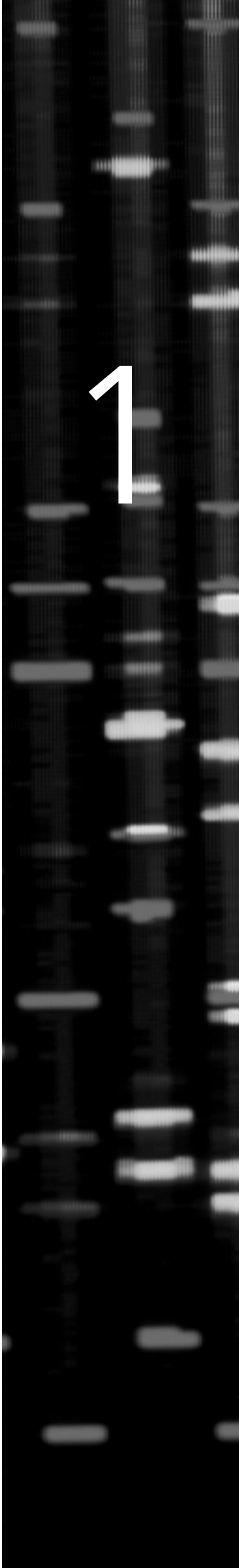
Chapter 1

Introduction



Introduction

1.1 The study of biology was radically transformed by the discovery in 1953 of the structure of DNA, which is the genetic material of living organisms (see Box 1.1). Since then, scientists have made considerable advances in understanding how DNA works, and how differences in DNA lead to differences between people. In 1990, the Human Genome Project was established to co-ordinate research that aimed to identify all the genes in human DNA, and to determine the order of the three billion chemical base pairs that make up human DNA. In 2001, the draft map of the human genome was published, which at least partially identified the majority of the estimated 30,000-40,000 human genes. Many of these genes play a role in human diseases and disorders. Their identification may be a first step in the development of new diagnostic tests and treatments. Research in the rapidly expanding field of genomics aims to discover the biological function of particular genes, and how sets of genes and proteins work together in health and disease. Research is also focusing on identifying and understanding the proteins produced by the genes.

1.2 Research into the sequence of the human genome has been undertaken jointly by publicly-funded bodies such as universities, charities, foundations and research institutes, and by privately-funded industrial organisations. Two versions of the map of the human genome sequence were published by the two communities of researchers, the data from the publicly-funded research having been incorporated into the privately-funded version.[1] The public sector project was conducted against the background of a strong commitment to the public sharing of, and access to data. All publicly-funded data regarding the draft sequence were placed on public databases as they were generated each day. In contrast, industry has generally treated DNA sequence data as confidential.

1.3 The protection of knowledge about human genes has primarily been achieved through the patent system, though other devices such as trade secrecy and confidentiality have also played a role.[2] The patent system is a long-established method of encouraging people to develop new and useful objects by ensuring that they are able to capitalise on their inventions. A patent confers on the inventor an exclusive right for a limited period of time (usually 20 years) to prevent others from exploiting the invention. Patents have been used for over a century to protect a wide range of inventions including new medicines, new materials and new machines. Naturally-occurring phenomena such as electricity or wild species of plants or animals are not regarded as inventions but as discoveries and thus are not eligible to be patented.

1.4 The substantial increase in the rate of patenting of DNA sequences by researchers in both the public and private sectors over the past six years has led to considerable discussion and debate about the acceptability of this practice.[3] The issue has been debated in numerous arenas and at

1 The public sector human genome project published the sequence in Nature (see Lander ES et al. Initial sequencing and analysis of the human genome. Nature 2001 Feb 15;409(6822):860-921); while the private sector project undertaken by Celera Inc, a US genomics company, was published in Science (see Venter JC et al. The sequence of the human genome. Science 2001 Feb 16;291(5507):1298-302).

2 The importance of secrecy as a method of protecting knowledge was highlighted by a recent survey of academic geneticists in the US which found that 35% of researchers felt that there had been a decline in the sharing of data in the past ten years. It also found that researchers who had been engaged in the commercialisation of university research were significantly more likely to withhold data from other researchers. The study concluded that the withholding of data in the field of genetics, though not widespread, was nonetheless affecting essential scientific activities such as the ability to confirm published results (see Campbell EG et al. Data withholding in academic genetics: evidence from a national survey. JAMA 2002;287:473-80).

3 See World Health Organisation. Advisory Committee on Health Research. Genomics and World Health. 2002. http://www3.who.int/whosis/genomics/pdf/genomics_report.pdf (7 Jun 2002).

Box 1.1: **Proteins, genes and DNA**

Genes are discrete segments of DNA molecules that contain the information necessary for producing specific proteins. DNA is made up of a string of units called nucleotides. The main component of these nucleotides are bases, which are arranged in a specific sequence. There are four different bases in DNA: adenine (A), thymine (T), cytosine (C), and guanine (G). These bases are bonded together in pairs, A with T and C with G, to make the DNA double helix. Genes can range in size from fewer than 100 base pairs to several million base pairs and are separated from one another by spacer DNA. The base sequence is the crucial feature of the gene. It is this sequence that carries the genetic information essential for the synthesis of an RNA molecule that may subsequently direct the synthesis of a protein molecule or may itself be functional in the cell. This process is called gene expression; it has two stages. The first stage in gene expression is transcription (the process by which the gene's DNA sequence is copied into RNA) and the second stage is translation (the process by which RNA directs the synthesis of a protein). Proteins are composed of amino acids and are the molecules that carry out the work of the cell. All the DNA in an organism is called the genome.

a range of levels. Patent law and practice has developed as a result of these debates. There remain, however, questions about the application of patent law with respect to DNA sequences and concerns about the potential consequences for society of allowing such patents. In 2000, the Nuffield Council on Bioethics convened a Round Table Meeting with the aim of producing a Discussion Paper that would clarify the issues raised and propose ways of taking the debate forward. This Paper is the result of nine meetings of the Round Table group, who were helped in their deliberations by experts in relevant fields from around the world. The subject which this paper tackles is necessarily technical and complex. It will be most readily accessible to those with an existing interest in, and knowledge of, genetics and the patent system.

Background to the current debate

1.5 Chemical compounds including medicines, chemical processes such as the polymerase chain reaction (PCR)[4] and medical devices such as the diagnostic test for hepatitis C have been the subject of patents for some time. Living organisms have also been the subject of patents. The modification of living organisms through genetic engineering in the 1970s and 1980s opened up new possibilities for the development of novel products and processes. By inserting foreign or synthetic genes directly into a bacterium, scientists were able to contemplate the creation of new drugs based on human genes, new crops and transgenic animals with new or enhanced properties.

1.6 Such developments rapidly led to an appreciation of the commercial possibilities arising from genetic modification and the advantages of protecting developments through the application of the patent system. Several hundred small biotechnology companies were established during the late 1970s and 1980s in the US to develop and apply the new genetic technologies. Many were founded within universities by entrepreneurial academics and later 'spun out' into the industrial sector. These developments in the life sciences, which were mirrored in other technologies, eroded the relatively clear divide between the publicly-funded sector of universities, research institutes and foundations, and industry. In 1980, the Bayh-Dole Act was passed in the US, which allowed universities and other public institutes and their employees to seek patent protection for their inventions and retain the royalties.

4 PCR is an *in vitro* method for generating unlimited copies of any fragment of DNA. PCR is useful for the characterisation and analysis of regions of DNA which lie between two regions of known sequence.

The same practice has, to a greater or lesser extent, been encouraged by the governments of many other countries. Thus the development of the new genetic technologies was accompanied by a changing culture in universities, where the pursuit of profit and patents took place alongside the more conventional academic activities of scholarship and the writing of books and scientific papers. These developments, encouraged by governments, have not been confined to the US. Universities around the world now have offices for intellectual property to encourage and facilitate the gaining of patent protection for the inventions of their faculty. Today, the owner of the greatest number of US patents that assert rights over genes is the US government, most of which have been generated by the National Institutes of Health (NIH) Intramural Research Program.[5]

1.7 Over the past 20 years, large numbers of genes, sections of genes and the proteins they produce have been the subject of several thousand patent applications. Many patents have been granted. The identification and cloning of genes that produce therapeutic proteins has led to the development of a number of new medicines based on human proteins[6], whilst the identification of genetic mutations that cause disease has been widely applied in the development of diagnostic tests for relatively rare diseases. Patents that assert property rights over DNA sequences have been granted in both these areas. Many pharmaceutical companies have invested in substantial research programmes to apply genetic knowledge to the process of drug discovery. With the completion of the sequencing of the human genome, many more patent applications for new drugs, vaccines and diagnostic tests involving the use of the estimated 30,000 - 40,000 human genes and their expressed proteins can be expected.[7] The market for medicines (in the form of therapeutic proteins) and vaccines is already significant.

1.8 Over the past decade, the idea that a gene or DNA sequence can be the subject of property rights as part of an invention and that the rights to the use of this alleged invention might rest with a single owner, such as a company, has attracted increasing criticism around the world. Researchers, clinicians, non-governmental organisations (NGOs), and religious groups have opposed, in particular, the idea that a DNA sequence can constitute part of an invention and therefore be claimed as property by the patent owner. This opposition seems to arise from anxiety about what might be termed 'private appropriation of the genetic commons'. We discuss this concern further in Chapter 3.

1.9 Concerns have been articulated relating to the effects of awarding exclusive rights, albeit time-limited, in this field. Four potential problems that may arise as a result of patents that assert rights over DNA sequences being granted are:

- 'preventing or hindering development of new or improved medicines and treatments;
- limiting access to healthcare by increasing the cost of diagnostic [tests] and treatment for certain diseases;

5 Cook-Deegan R. Gene patents - why secrecy is destructive to innovation. In: Commercialization of genomics: challenges and opportunites. Cambridge, MA: Cambridge Healthtech Institute; Dec 2001. p. 59. Furthermore, some public sector grant-giving agencies require the researchers they fund to seek protection for their intellectual property.

6 For example, erythropoietin (Epo), granulocyte colony-stimulating factor (G-CSF), tissue plasminogen activator (t-PA) and human growth hormone.

7 In 2000, the Guardian newspaper published a report on patenting which included estimates of the number of patent applications filed that assert property rights over DNA sequences, based on research commissioned from GeneWatch UK. The newspaper stated that 'Patents are already pending or have been granted on more than 50,000 genes and partial gene sequences in living organisms.' (See Meek J. The race to buy life. In: The Guardian. 15 Nov 2000. http://www.guardian.co.uk/genes/article/0,2763,397827,00.html (30 May 2002).)

- exploiting information and materials and inhibiting their free exchange between researchers;
- involving parties in extensive and costly legal battles.'[8]

Conversely, it has been argued that patents on DNA are necessary to stimulate investment in research and development on new healthcare products and processes, to assure protection in the market for new products and to facilitate the disclosure of scientific information. This paper critically assesses these arguments.

1.10 The joint statement which the Prime Minister of the UK, Tony Blair, and the President of the US, Bill Clinton, made on 14 March 2000, reflected the tension between the calls for openness and access to data on the human genome and the calls for the protection of data to facilitate commercial development. The statement declared that 'raw fundamental data on the human genome, including the human DNA sequence and its variations should be made freely available to scientists everywhere'.[9] But, it also recognised the importance of intellectual property, noting that 'intellectual property protection for gene-based inventions will also play an important role in stimulating the development of important new healthcare products'.

Background to this Discussion Paper

1.11 Various bodies have been or are engaged in work to assess the ethical implications of patenting DNA and to consider reform of current patent systems. The United Nations, through its Convention on Biological Diversity signed in 1992, placed strong emphasis on the fair and equitable sharing of benefits arising from the use of genetic resources. The Council of Europe has since proposed collaborating with the European Union (EU), World Intellectual Property Organisation (WIPO), Food and Agriculture Organisation, World Trade Organisation (WTO) and United Nations Educational, Scientific and Cultural Organization (UNESCO) to discuss a suitable alternative system of protecting intellectual property in relation to biotechnology which would meet the aims of the Convention on Biological Diversity and global interests, both public and private. Work is also continuing on the section of the Council of Europe's additional protocol of the Convention on Human Rights and Biomedicine devoted to the consideration of issues raised by the human genome.

1.12 The aim of this Discussion Paper is to examine the issues relating to genetics and intellectual property, particularly those that concern human healthcare and research related to healthcare. The objectives of the Round Table Meeting were:

- to examine ethical and legal issues within the current regulatory framework;
- to provide an ethical framework and policy recommendations to assist policy-makers and others, particularly the courts, patent lawyers and patent offices.

The Round Table Meeting did not consider a number of related issues such as the question of access to medicines in developing countries, or wider questions about intellectual

8 Patenting genes - stifling research and jeopardising healthcare. GeneWatch UK Apr 2001.

9 Prime Minister Blair, President Clinton. Joint statement to ensure that discoveries from the human genome are used to advance human health. 14 Mar 2000. http://www.patent.gov.uk/about/ippd/notices/genome.htm (13 May 2002). The Blair/Clinton statement was compatible with the Bermuda statement which set out guidelines for the release of DNA sequence data from genome centres participating in the international Human Genome Project. Participating centres were required to release their data from high-throughput screening on a daily basis.

property and the developing world. Nor did the group consider the patenting of DNA outside biomedicine, for example in relation to food and crops.

1.13 The structure of the Discussion Paper is as follows. Chapter 2 describes the justification advanced for the patent system and explains how the system functions. Chapter 3 explains how patents can assert rights over DNA sequences and examines the question of whether DNA should be patentable. It also summarises the current legal situation in the UK, Europe and the US, with regard to the patenting of DNA sequences. Chapter 4 contains five case studies that illustrate the possible effects of allowing patents that assert rights over DNA sequences. Chapter 5 considers the effects of such patents in more detail and proposes ways of modifying the patent system to ensure that it continues to work for the benefit of all. Chapter 6 summarises our conclusions and recommendations.