already been granted for human genes, 10 for animal genes and 9 for plant genes[30]. Therefore, whilst Blair and Clinton try to look good in public, they are in fact presiding over the wholesale monopolisation of genetic information, the stifling of research in the public sector and the restriction of the benefits of genetic research to the wealthy.

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PRIVATISING KNOWLEDGE, PATENTING GENES:
The Race to Control Genetic Information

GeneWatch UK

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A race is underway to control the genetic information (genomes) of humans, plants and animals. Private companies are vying with each other and with the public sector to be the first to identify genes and what they do. Fierce arguments are taking place over how such information should be protected – should data about genes be freely available or should genes be patentable? Companies insist that they must have the monopoly rights which patents bring if they are to recoup their investments in research and development. Many public sector scientists oppose patents on genes, believing they will obstruct rather than stimulate research. Others believe that patenting genes and organisms is simply immoral. This briefing examines the issues behind the control of genetic information and considers how the public interest should be protected.

The Genome Research Race

The genome of an organism is all the genetic (hereditary) information it contains. Identifying its constituent genes and what they do potentially enables the production of new genetically modified crops and animals with improved production efficiency and the development of new drugs and treatments. The benefits and profits from genome research could therefore be huge and consequently there is enormous interest in gene mapping in the private and public sectors. How knowledge of the genomes of organisms is shared or controlled will be vital in determining who will benefit.

Following early studies of several microorganisms and a soil worm to work out the order of the chemical letters making up their genomes (a process known as sequencing), there are now both public and private sector projects to sequence the genomes of many higher organisms including humans, mice, zebra fish, fruit flies, rice and maize. Human genome research has attracted the largest investment. The aim of the international, publicly funded $3 billion Human Genome Project (HGP) is to map the human genome by 2003 although a 'first draft' is expected in 2000[1]. The UK's contribution at the Sanger Centre in Cambridge is receiving funding of approximately $450 million over ten years from the Wellcome Trust.

However, specialised private 'genomics' companies such as the US based Celera Genomics, established by Craig Venter, are trying to sequence the genome even faster. Using a combination of its own data and public data, Celera claim to have sequenced 90% of the human genome already and predict they will have completed it by the summer of 2000[2]. Other leading genomics companies include the US based Human Genome Sciences and Incyte, which recently acquired the UK company Hexagen and is investing $200 million in sequencing efforts over two years alone. These genomics companies plan to sell their data to others and already have agreements with many large drug companies. However, the pharmaceutical industry is concerned that these specialised genomics companies are more advanced in sequencing than their own organisations. As a result, a consortium has been formed by ten major pharmaceutical companies - including Bayer, SmithKline Beecham and Hoffman-La Roche with the medical charity the Wellcome Trust - to map genetic variation and has a $47 million budget over two years[3]. (A recent publication by the Canadian group, RAFI, gives more details of companies and alliances in human genomics.[4])

Similar competition is taking place in the genome mapping of non-human organisms, albeit with lower overall investment. With plants, there are international, publicly funded

projects to map the genomes of *Arabidopsis* (thale cress, an important research plant) and rice. There are also many national public projects. In the private sector, all the major life sciences corporations have both their own in-house crop genome mapping projects and agreements with specialised genomics companies. For example, Monsanto has interests in genome research in soybean, rice and maize; DuPont in maize, wheat, soybean, and rice; and Novartis in rice, maize and wheat. Celera Genomics claims it can map the genome of rice in six weeks[5]. Private-public partnerships in plant genomics research also exist. (The Barcelona based organisation, GRAIN, has recently detailed the key institutions involved in plant genomics.[6])

Sequencing animal genomes lags behind that of humans and plants. There is an international, public effort to sequence the laboratory mouse genome because of the potential spin-off knowledge for medical research. Celera Genomics intends to map the mouse genome for the same reason. However, with domestic species, efforts to map the pig, cattle, sheep and chicken genomes[7] are relatively low-key because of the low commercial value of the animal breeding and animal health industries[8].

Recently, there has been much controversy about whether the sequences of DNA molecules that are discovered in genomics research should be published and freely available, whether they should be patentable or whether access to the data should only be allowed subject to some contractual arrangement.

Patents are powerful tools through which the control of the genomes of staple food crops, animals and humans are falling into private hands

What are Patents?

Patents give the inventor (the patentee) a monopoly right to the commercial exploitation of their invention for 17 years. In exchange, the patentee describes the invention in the patent, which is then available to anyone. The theory is that by disclosing details of the invention, the knowledge can be shared and so stimulate further research and innovation whilst allowing the inventor to commercialise the invention without their idea being stolen and copied.

Patents allow the patent holder to determine how and whether an invention can be used and by whom. A patent holder may exploit an invention, sell exclusive or non-exclusive licences at a negotiated fee, or leave an invention unexploited. The primary motivation for such decisions will be how to maximise profits, the size of potential markets and the actions of competitors. Public interest is of little consequence in the decision making process.

To be patentable, an invention must fulfil three basic requirements:

- be inventive (i.e. is not a discovery);
- have novelty (i.e. is not obvious);
- have industrial applicability.

Until recently, patents were restricted to inanimate inventions such as new engines, vacuum cleaners, drugs, or processes for producing chemicals. The first patent on a living organism was awarded in the USA in 1980 for a microorganism that could degrade oil. Gradually, the scope of patentability has been extended in the USA and Europe to include higher plants and animals. A patent on a gene or DNA sequence covers anything which is derived from it and, as a result, may extend to all plants, animals, microorganisms, drugs or diagnostic test kits which have been developed with the aid of the patented gene. Therefore, patents are powerful tools through which the control of the genomes of staple food crops, animals and humans are falling into private hands.

increasingly important research targets. Biopiracy could affect us here rather than being a distant issue. Already, an American - John Moore - has found that his spleen cells have been patented without his permission after his spleen was removed during an operation. Many other undiscovered examples may also exist and the problem will intensify.

Private companies are already involved in large-scale sampling in the developed world in the search for useful genes. For example, DeCODE Genetics have successfully negotiated with the Icelandic Government for exclusive access to the medical histories and tissue banks of all 270,000 Icelanders[3]. Hoffman-La Roche have agreed to pay up to $200 million for deCODE's Icelandic data on genetic causes of twelve common illnesses including diabetes and Alzheimer's disease. In Estonia, a similar project is being planned as a public/private collaboration between the Genome Center and deCODE Genetics[25].

There are no comprehensive regulations covering the use of genes or tissues obtained from samples in human tissue banks

Publicly owned and funded tissue and cell banks held in many universities and research institutions in the UK are available to both private and public researchers and will be important sources of genetic material. A joint venture between the Medical Research Council (MRC) and the Wellcome Trust working with the National Health Service to establish a 'UK Population Biomedical Collection' is expected to be announced soon[26]. This is intended to be the UK's major resource in investigating the role genes play in health and disease. It will aim to collect samples from up to half a million people, probably aged 45 - 65, although *"[i]ssues of 'ownership' of samples and data, and of accessibility of data, will have to be solved"*.[27]

In fact, there are no comprehensive regulations covering the use of genes or tissues obtained from samples in human tissue banks. Only now are voluntary guidelines starting to be updated in the light of developments in genetics. Whilst donors should be informed that private companies may have access to tissue they have freely given, if proposed MRC guidelines for the management of tissue banks are implemented[28], this will be explained in the context of the importance of encouraging research and development by private companies.

Conclusions

An important consequence of allowing the private control of genetic information is that public interest research will suffer and benefits will be restricted to those who are able to afford them. As Bruce Alberts, president of the US National Academy of Sciences, and Aaron Klug of the Royal Society have said: *"..to work effectively and bring widespread benefits as quickly as possible, it is vital that all researchers have access to the full genome without charge or other impediment. The human genome itself must be freely available to all humankind"*.[29]

Blair and Clinton are presiding over the wholesale monopolisation of genetic information, the stifling of research in the public sector and the restriction of the benefits of genetic research to the wealthy

Furthermore, patents are being used to plunder the knowledge and genetic resources of peoples in both the developed and developing world, often without the full consent of the people or nations involved.

Despite the intervention of Blair and Clinton, nothing will change unless there is a ban on the patenting of genes, plants and animals and safeguards introduced to ensure that material used from publicly held tissue banks cannot be subject to intellectual property claims by researchers or companies. Instead, however, the UK Government is in the process of amending UK law to explicitly allow the patenting of genes, cells, plants and animals for the first time. According to the UK Patent Office, approximately 50 patents have

much of the world's biodiversity and companies hope to find compounds they can use as drugs or genes they can use in new crop developments.

Exploitation of local individuals and communities is a real danger. Although identifying which plants may be useful as medicines often relies on the knowledge of local people, this is rarely acknowledged. Some examples of biopiracy and bioprospecting for plants include (see also GeneWatch Briefing No. 3):

- Mars UK has two US patents (US 5,770,433 and 5,668,007) on genes from a West African cocoa plant (*Amelonado* sp.) which are thought to be responsible for the distinctive cocoa flavour associated with the region[19]. Mars could develop the work to manufacture substitutes for cocoa, thus depriving cocoa producing countries of essential export income.
- A US company, Pod-Ners, has sued Mexican bean exporters for allegedly infringing their patent (US 5,894,079) on a yellow bean variety by importing yellow beans into the USA[20]. However, the yellow bean patented by Pod-Ners originates from the 'Azufrado' variety of beans bought by the company in Mexico in 1994. Pod-Ners is also demanding royalties of six cents per pound on the imported beans.
- The US Government is funding bioprospecting projects for plants, fungi and insects in partnership with pharmaceutical companies including Monsanto, American Home Products, Glaxo-Wellcome and Bristol-Myers Squibb in Mexico, Panama, Madagascar, Suriname, Peru, West Africa, Vietnam, Laos, Argentina and Chile[21].
- India has been a special target of bioprospectors. Relying on local knowledge of their medicinal and other properties, patents have been applied for on plants including turmeric, pepper and the neem tree, causing outrage among local growers[22].

There is little realistic prospect of research being targeted at the needs of those in the developing countries who have donated the genetic resources

Biopiracy of Humans

Bioprospecting for human genes and tissues is part of the Human Genome Diversity Project (HGDP), a part of the Human Genome Project. The HGDP extends the mapping efforts to understand the *function* of genes ('functional genomics'). By understanding what a gene does, it can then be exploited in, for example, the development of medicines. By looking at differences between people - whether they do or don't contract a particular disease, for example - genes responsible for the differences can be identified. This will demand a considerable effort to collect samples, identify differences in genes and equate these with physical, biological or psychological abnormalities. A whole range of different races, patient groups and individuals will have to be sampled – hence the HGDP.

However, the HGDP has been criticised for targeting ethnic groups around the world and has been accused of exploiting indigenous peoples[23]. When samples are taken, many people have been given little or no information about the project. There is also little realistic prospect of research being targeted at the needs of those in the developing countries who have donated the genetic resources or local people being able to have access to any medicines developed using the knowledge. Although the future of the HGDP is currently in question due to lack of funding[24], less visible nationally and privately controlled projects continue to sample ethnic groups[4].

Although biopiracy has been associated mainly with the appropriation of biological materials from developing countries or minority groups, as functional genomics develops, groups and individuals in the developed world will be

What's Wrong with Patenting Genes?

A whole array of criticisms have been levelled against the patenting of genes and living organisms including:

- genes exist in nature and cannot be considered to be 'inventions';
- claiming to have invented genes and organisms is immoral;
- allowing the control of genetic information and how it is used to fall into private hands is dangerous;
- there is no evidence that patents actually encourage innovation and that they may even be used to prevent or discourage research because of concerns about royalty charges and legal challenges;
- a new form of genetic imperialism could arise if companies from rich countries claim patents on genes found in developing countries - so-called biopiracy.

Some of these issues are explored below.

Privatising Knowledge

Fears that the private sector is gaining control of the human genome and particularly that Celera Genomics will gain a monopoly over human genome data, has led to a furious debate. Celera's aggressive patenting policy and refusal to lodge data with the public database, GenBank, to avoid competitors having access[9,10], prompted Prime Minister Tony Blair and President Bill Clinton's recent call for human genetic information to be freely available[9].

The primary objection (mainly from public sector scientists) to allowing genome sequences to be patented is that this is basic scientific data and gives no information about what genes do and so, by definition, should not be patentable. However, whilst the HGP plans to make its sequence data freely available - as do some commercial organisations, including even Monsanto with its rice genome mapping data[11] - Celera Genomics filed preliminary patent applications on 6,500 partial human gene sequences in October 1999.

Even when genome sequences are made available by commercial companies, there are strings attached. Sometimes payment is required for access to such data and Celera, for instance, offered rice genome data to companies for a $30 million, five-year access contract[5]. If the information is subsequently used in product development, payment to the company which carried out the original genome mapping may also be required.

Even when genome sequences are made available by commercial companies, there are strings attached

In the case of genes whose functions have been determined, private companies are all insistent that patents should be awarded. The US Patent Office has already granted over 1,500 patents on human genes[3] and many thousands more are in the pipeline. For example, by October 1999, Human Genome Sciences had filed patents for over 6,400 full human gene sequences.

Food crops are also coming under corporate control. Of 601 patent applications for genes from plants, almost three quarters were filed by private companies and only 28% were from public sector institutions[12]. Other research shows that all the world's staple food crops are now being patented[19].

The US Patent Office has already granted over 1,500 patents on human genes and many thousands more are in the pipeline

Encouraging Innovation or Stifling Research?

The basic premise of intellectual property rights (IPRs), including patenting, is that innovation will be stimulated and competitiveness encouraged. However,

Patent Law

Every country has its own legislation to grant national patents and there are also regional agreements such as the European Patent Convention (EPC). Under the EPC, a single application to the European Patent Office (EPO) in Munich results in a patent being recognised across Europe. There is also one international UN agency dealing with patents - the World Intellectual Property Organisation (WIPO) - where companies can register their claims, although these have to be approved by individual national patent offices. Although the WIPO does not actually assess the validity of a patent application, its publication by them serves to prevent anyone else patenting the invention in a listed country. Therefore, a patent may cover one country, a region or large sections of the world.

European

The EPC specifically excludes plant and animal varieties, processes which are essentially biological, and inventions which are contrary to morality from being patented. Because companies are anxious to gain full patent protection on genetic technologies, they want these exclusions removed. Consequently, even though the EPC is not an EU treaty (as it includes non-EU nations such as Switzerland), the EU was persuaded to introduce a Directive to allow the patenting of biotechnological inventions. The first time the Directive was introduced, it allowed for patents on genetic material, plants and animals and was rejected by the European Parliament in 1995. However, a revised Directive (98/44/EEC) was agreed in 1998 when certain safeguards were introduced, such as the clarification of inventions which would be considered immoral (including cloning of humans and germ line gene therapy) and the inclusion of a 'farmers' privilege' (to allow seed to be kept for future years). But the major factor which caused the European Parliament to change its mind about the Directive was the concern - promoted by the pharmaceutical companies - that unless such patents were allowed, medical research might be compromised.

To allow patenting of genes (which are discovered during scientific research and so should not qualify as they are not invented), the Directive was worded so that if there had been some 'technical' process involved, this then becomes 'inventive'. Since all gene sequencing and identification involves some technical intervention, no bar to patenting genes exists if some description of their function and possible use is given.

Despite the agreement of a Directive on patenting in the European Union, the situation is far from being clarified because European Directives are not legally binding on the EPO. In October 1998, the Dutch Government (supported by Italy but opposed by France) challenged the legality of the Patenting Directive at the European Court of Justice because, in part, of this conflict with the EPC. The ruling of the Court of Justice is expected shortly.

The UK, like other EU countries, is now implementing the European Directive. The proposed changes to UK law will explicitly allow the patenting of genes, cells, plants and animals for the first time.

Global

Internationally, the European approach to patenting biotechnological inventions also has to be consistent with the TRIPS agreement (Trade Related Aspects of Intellectual Property Rights). According to the TRIPS Article 27.3(B), members of the World Trade Organisation (WTO) must have either a patent system or some other system for intellectual property rights which they believe is appropriate (an "effective *sui generis* system"). The USA and some other developed countries are opposed to this provision and are advocating a universally enforced patenting system. Article 27 of the TRIPS agreement was to be reviewed at the WTO meeting in Seattle in 1999 but this did not happen. Many less developed countries do not want the review to go ahead, believing it will be used to remove their rights to have a locally appropriate patent system and to exclude the patenting of biological materials if they so wish.

Proposed changes to UK law will explicitly allow the patenting of genes, cells, plants and animals for the first time

Evidence is emerging that patents on genes are actually hindering research in the public sector and creating monopolies on their use

evidence is emerging that patents on genes are actually hindering research in the public sector and creating monopolies on their use that will restrict their availability and may make medical products prohibitively expensive. For example:

- Research into screening methods and treatments for genetic diseases is being stifled by patents on genes. A survey of US public sector laboratories in 1999 found that 25% had received letters from lawyers of biotechnology companies ordering them to stop carrying out many clinical test research programmes including those designed to identify Alzheimer's disease and breast cancer[13].
- In 1998, the Manchester Regional Genetics Centre was billed for $5,000 by a Canadian biotechnology company for the use of a cystic fibrosis kit. At the time, Dr Gareth Evans, a consultant at Manchester, warned that *"Genetic tests for heart disease and breast cancer may involve testing of 15 or more genes each. This will mean 15 separate royalties will have to be paid"*.[14]
- In 1999, Myriad Genetics claimed royalties from the National Health Service for developing their own test kits for human breast cancer susceptibility genes, BRCA1 and BRCA2. Myriad had patented these gene sequences even though their research had relied upon work by the Institute of Cancer Research in London. If forced to pay a licence fee to Myriad, Shirley Hodgson of Guys Hospital has said: *"[in] theory, it could completely cripple a lot of labs"*.[15]
- A 1999 survey of public sector plant breeders in the USA showed that intellectual property protection was hindering their work[16]. 48% of those replying to the questionnaire had had difficulties getting genetic stocks from private breeders, 45% said this had interfered with their research, and 23% said it had interfered with the training of students.

Patent battles between companies reveal that broad patents are being claimed on the use of genes and basic laboratory methods that may create unfair monopolies inside the private sector. A US biotechnology company, Amgen, that owns the patent for the human erythropoietin (EPO) gene is challenging Transkaryotic Therapies' (TKT) production of EPO even though TKT claim it is using a different technique that does not rely on the EPO gene. One expert has commented that "*If Amgen prevails, it suggests that US patents are so restrictive that it would actually discourage legitimate innovation*"[17]. In another case, an Oxford professor, Ed Southern, has claimed that a company called Affymetrix is using patents to create a *"stranglehold"* over 'microarray' technology used to determine which genes are switched on and off[18].

Therefore, far from stimulating research and innovation, patents on genes and associated basic technologies may not only hinder public sector research but act against competition in the private sector.

Biopiracy of Plants

One controversial area of genomics research is the so-called biopiracy of natural genetic resources. This is when freely available genetic resources are taken - very often from developing countries by companies or institutions of developed countries - and genes, cells or even whole organisms are patented and claimed as inventions. The search for useful genes - 'bioprospecting' - in developing countries is high on research agendas as these countries contain