A UK Intellectual Property Office (UK-IPO)

Technology Report

on

GENOMIC MEDICINE

A Response to the Call for Evidence of the House of Lords Select Committee on Genomic Medicine

April 2008

Executive Summary

The UK Intellectual Property Office (UK-IPO) is responsible for the policy framework and the administration of intellectual property rights (IPRs) in the UK.

As part of DIUS[1] Science and Innovation Group the Office is committed to playing an important role in creating the conditions so that the maximum economic and social benefit can be extracted from IP. This includes making the best use of patent data to support innovation.

The IPO is pleased therefore to support the House of Lord's Select Committee on Science and Technology enquiry into Genomic medicine in the UK. Patenting is a key marker of innovative activity and provides a useful early insight into what technologies are developing and may emerge in the market-place.

In this report we provide information in response to four areas detailed in the Call for Evidence[2] (See Annex 1): We outline the policy framework for patents concerning Genomic Medicine noting the restrictions and variations regarding what can be patented in the medical field[3] internationally. The report then provides a detailed analysis of the genomic medicine patent landscape using information of patent records from all major industrialised countries. The approach taken was to analyse the field of Genomic Medicine in terms of patents filed for inventions in eight areas of technology which feed directly into the development of this filed. These were:

- **Gene expression profiles**
- **Human genes**
- **Genes and regulatory sequences**
- **Protein-protein interactions**
- **SNP/haplotypes**
- **Gene-related Algorithms/software**
- **Modified animals**
- **Protein structure**

This data was then used to respond to the questions from the Call for Evidence (see Chapters 4-9). Finally, in Chapter 10, the patent landscape in relation to a cancer diagnosis and prognosis was considered.

The report shows:

[1] Department of Innovation, Universities & Skills (DIUS)

[2] http://www.parliament.uk/parliamentary_committees/lords_s_t_select/genomic.cfm

[3] There are some differences between the US and Europe in relation to what types of inventions involving computer software, algorithms and/or databases are considered to be patentable

- Genomic Medicine is an area of interest that is attracting significant interest worldwide. The leading pharmaceutical companies from US, Europe (Germany, France, UK and Switzerland) and Japan are all involved to a significant degree in filing patent applications in all the relevant areas of research. Chinese companies have begun to emerge as a significant player, especially in the area of **human gene** patents.

- A significant body of world-wide patent filings relevant to Genomic Medicine derives from UK based pharmaceutical and biotechnology companies.

- The top five UK based patent applicants in Genomic Medicine are GLAXOSMITHKLINE, ASTRAZENECA, SYNGENTA, ICI and the MEDICAL RESEARCH COUNCIL (MRC)

- The breadth and diversity of UK based research activity in Genomic Medicine is demonstrated by the 161 UK patent applicants including 116 companies, 29 universities and 16 public research bodies/ charities.

- It is clear that UK academia displays a significantly higher proportion of patenting activity than the world in general. However, the UK hospital sector does not.

- There is an intense web of collaboration giving rise to IP relevant to Genomic Medicine, usually involving multiple publicly-funded bodies, such as universities, and often an industry partner. UK corporate and university entities show a significant level of international collaboration. Noticeable collaboration is also occurring between entities in the UK. All types of collaboration are seen, i.e., academic-corporate, academic-academic and corporate-corporate.

- By all measures examined, the UK has a high profile in Genomic Medicine. UK involvement in this field displays a good cross-section of representatives from all business sectors including large pharmaceutical companies, smaller biotechnology companies, universities and public sector research institutes.

- Worldwide and UK Academic/research sector applicants lead in the area of **modified animal patents,** whereas Worldwide and UK Corporate sector applicants lead in the seven other areas of technology searched.

- Two of the areas of technology searched - **Gene expression profiles** and **SNPs/haplotypes** – which concern the detection of alterations in DNA or RNA expression in the individual that can lead to disease have very important diagnostic applications. Both these areas show strong performance by UK corporate entities. GlaxoSmithKline is the leading patent applicant worldwide in the area of **Gene expression profiles.** GlaxoSmithKline, AstraZeneca and ICI are leading applicants (within the top 14) in the area of **SNPs/haplotypes.**

CONTENTS

LIST OF TABLES

Chapter 1: Introduction

Reference to "patents" throughout the report relates to both patent applications and granted patents unless otherwise indicated

1. Structure of the Report

In Chapter 2 the report defines Genomic Medicine and considers its relationship to the wider field of Genomics.

Chapter 3 contain an outline of the policy framework within which patents concerning Genomic Medicine can be obtained. This includes a discussion of the restrictions regarding what can be patented in the medical and genetic fields. Also there are some differences between the US and Europe in relation to what types of inventions involving computer software, algorithms and/or databases are considered to be patentable

Chapters 4-9 represent the main body of the report. Each of these chapters discusses a different question from the Call to Evidence issued by the House Of Lords Select Committee on Genomic Medicine[4]. The data used to discuss and answer these questions is obtained from an analysis of the genomic medicine patent landscape. Chapter 10 looks specifically area that will be relevant to the area of patents applied for

Annex 1 list the questions from the call of Evidence that the report answers. Annex 2 provides information on some of the data analysis methodology used.

The Annexes to Chapters 6, 7 and 10 contain further information, tables, and figures referred to in the main text of these Chapters. The conclusions drawn in this report are based on the data in the Annexes as well as that presented in the Chapters of the report

2. Analysis of Patent Data

For this study we used the EPODOC database developed and maintained by the European Patent Office (EPO) as the source of patent related data. The EPODOC database encompasses published patent documents derived from the majority of leading industrialised countries and patent organisations, for example the World Intellectual Property Organisation, EPO and the African Regional Industry Property Organisation (ARIPO).

Patent applications are usually published 18 months after the patent has been applied for. Not all of these applications will go on to be granted patents, for example, an applicant may allow a published patent to lapse or may withdraw

[4] see footnote 2 for full details of the Call to Evidence

it, or the application may not successfully complete the appropriate patent grant process.

Although our search looked at patent data from 1995 to 2007, we have only presented data for the period 1995 to 2006 in this report. The data obtained for 2005 to 2007 is much less reliable than the data for the period 1995 to 2005. As patents are usually published eighteen months after filing, the data reflects the time when the information became available rather than when the research was carried out. Thus the data for 2005 may be incomplete and that for 2006 and 2007 is incomplete.

A further limitation to note is that it can take up to a period of 2 years from the date of that a patent application is made (or filed) for the invention described in each patent application to be fully classified and so available for searching using databases such as EPODOC.

Further details regarding the methodology used for the analysis of the patent data are provided in Annex 3.

3. Analytical Tools used

The UK-IPO utilises patent information analysis software supplied by Thomson Scientific. The data presented in this report was generated using Thomson Data Analyser (TDA).

Chapter 2: What is Genomic Medicine?

Genomic Medicine is best understood by first considering what is mean by the term genomics and then considering the particular role of genomics in medicine.

1. Genomics

Genomics is the study of an organism's entire genome[5]. This field includes efforts to determine the entire DNA sequence and gene map of organisms. In contrast, the investigation of single genes and their functions and roles, a common part of today's medical and biological research, does not fall into the definition of genomics. However, genomics does include genetic, pathway, and functional information analysis designed to elucidate the effect on and response of the entire genome's networks.

Genomics is an area of research that has grown very rapidly since it the first gene sequence was published in 1972. This is summarised in Table 1. The culmination of this work has been the publishing last year of the genome sequence of two individuals who have been very influential in the development of this science, James D Watson and J Craig Venter.

Many genomes have been sequenced by various genome projects since 1972. As of September 2007, the complete sequence was known of at least 1879 viruses, 577 bacterial species and roughly 23 eukaryote organisms, of which about half are fungi[6]. Most of the bacteria whose genomes have been completely sequenced are problematic disease-causing agents, such as *Haemophilus influenzae*. Of the other sequenced species, most were chosen because they were well-studied model organisms or promised to become good models. Yeast (*Saccharomyces cerevisiae*) has long been an important model organism for the eukaryotic cell, while the fruit fly *Drosophila melanogaster* has been a very important tool (notably in early pre-molecular genetics). The worm *Caenorhabditis elegans* is an often used simple model for multicellular organisms. The zebrafish (*Brachydanio rerio)* is used for many developmental studies at the molecular level and the flower *Arabidopsis thaliana* is a model organism for flowering plants. The Japanese pufferfish (*Takifugu rubripes*) and the spotted green pufferfish (*Tetraodon nigroviridis*) are interesting because of their small and compact genomes, containing very little non-coding DNA compared to most species. Mammals such as the dog (*Canis familiaris*), brown rat (*Rattus norvegicus*), and mouse (*Mus musculus*),

[5] **Genomics** was established by Fred Sanger, a UK biochemist working in Cambridge, when his research group first sequenced the complete genomes of a virus and a mitochondrion. His group established techniques of sequencing, genome mapping, data storage, and bioinformatic analyses in 1970-1980s.

[6] For up-to-date information regarding the number of genomes that have been sequenced please see the website of the US National Institutes of health at http://www.ncbi.nlm.nih.gov/genomes/static/gpstat.html

are all important model animals in medical research, while the chimpanzee (*Pan troglodytes*) genome is of great interest as our closest living relative.

It is important to note that a genome does not capture the genetic diversity or the genetic polymorphism of a species. For example, the human genome sequence in principle could be determined from just half the information on the DNA of one cell from one individual. To learn what variations in genetic information underly particular traits or diseases requires comparisons across individuals. This point explains the common usage of "genome" (which parallels a common usage of "gene") to refer not to the information in any particular DNA sequence, but to a whole family of sequences that share a biological context.

Table 2.1: 25 years Progress in Genome sequencing – 1972 to 2007

Year	Genome	Comments
1972	The first sequence of a gene published – the gene for Bacteriophage MS2 coat protein	Walter Fiers, Ghent, Belgium
1976	The complete nucleotide sequence of a viral genome was published for Bacteriophage MS2 RNA	Walter Fiers, Ghent, Belgium
1977	The first DNA based genome to be sequenced in its entirety was that of bacteriophage Φ-X174; (5,368 bp)	Frederick Sanger, Cambridge UK
1995	The first free living organism to be sequenced was the bacterium *Haemophilus influenzae* (1.8 Mb)	Robert Fleischmann, The Institute for Genomic Research (TIGR), USA
2000	A rough draft of the human genome was completed	Announced jointly by US president Bill Clinton and British Prime Minister Tony Blair on June 26, 2000
2003	Ongoing sequencing led to the announcement of the essentially complete genome in April 2003	
2006	The sequence of the last chromosome was published in the journal Nature.	
2007	The complete DNA sequence of a single individual published for the first time.	The DNA sequences of Craig Venter and James D Watson both published in 2007

A major branch of genomics is still concerned with sequencing the genomes of various organisms, but the knowledge of full genomes has created the field of functional genomics, which is mainly concerned with patterns of gene

expression[7] during various disease conditions. The most important tools for this purpose are (a) biological assays referred to as microarrays and (b) bioinformatics.

In May 2007, the *New York Times* announced that the full genome of DNA pioneer James D. Watson and that of human genome project pioneer J Craig Venter were being made available for scientists to study.[8] The article noted that some believe that individual genome mapping is the gateway to personalized genomic medicine. Knowledge of an individual persons genome will help a great deal in identifying susceptibility to ceratin disease conditions and likely reactions to therapy and treatment. The article also noted that Dr. Watson said that he will make his entire genome available for researchers to study, with the single exception of his apolipoprotein E gene, the status of which he does not wish to know because it may predispose a person toward Alzheimer's disease.

2. Genomic Medicine

In an article in the New England Journal of Medicine in 2002[9], Genomic Medicine was defined in the following manner:

> "If genetics has been misunderstood, genomics is even more mysterious - what, exactly, is the difference? Genetics is the study of single genes and their effects. "Genomics", a term coined only 15 years ago, is the study not just of single genes, but of the functions and interactions of all the genes in the genome. Genomics has a broader and more ambitious reach than does genetics.
>
> The science of genomics rests on direct experimental access to the entire genome and applies to common conditions, such as breast cancer and colorectal cancer, human immunodeficiency virus (HIV) infection, tuberculosis, Parkinson's disease, and Alzheimer's disease. These common disorders arise from the interactions of multiple genes and environmental factors. They are thus known as multifactor disorders.

---

[7] **Gene expression** is the process by which inheritable information from a gene, such as the DNA sequence, is made into a functional gene product, such as protein or RNA. Several steps in the gene expression process may be modulated, including the transcription step and the post-translational modification of a protein. **Gene regulation** gives the cell control over structure and function, and is the basis for cellular differentiation, morphogenesis and the versatility and adaptability of any organism. Gene regulation may also serve as a substrate for evolutionary change, since control of the timing, location, and amount of gene expression can have a profound effect on the functions (actions) of the gene in the organism.

[8] The New York Times, May 31, 2007 see http://www.nytimes.com/2007/05/31/science/31cnd-gene.html?_r=2&em&ex=1180843200&en=19e1d55639350b73&ei=5087%0A&oref=slogin&oref=slogin

[9] New England Journal of Medicine, Volume 347, pp 1512-1520 November 7, 2002, Number 19 see http://content.nejm.org/cgi/content/full/347/19/1512

> Genetic variations in these disorders may have a protective or a pathologic role in the expression of diseases."

With all of the above in mind, the definition of Genomic medicine that the UK-IPO has used for the purposes of this report is the application of the expanding knowledge of the human genome to medical practice. The essential foundation of Genomic medicine is Genomics which for the purposes of this report is defined as the study of the functions and interactions of all the genes in the genome, including their interactions with environmental factors.

Chapter 3: The Policy Framework

This chapter considers the questions in the Call for Evidence related to the Policy Framework for Genomic Medicine in so far as it relates to the granting of patents in this area of technology (see Annex 1).

Patenting Policy & Genomic Medicine

The UK Intellectual Property Office is responsible for setting and reviewing policy on intellectual property rights. The UK-IPO works with other Government departments, notably Department for Innovation, Universities and Skills, the Department of Health and the Department for Business, Enterprise and Regulatory Reform, and external stakeholders in advising Ministers on policy in relation to the patenting of genes.

Under UK law, genes as they exist in the cells in human bodies cannot be patented. This is because patents are not available for discoveries. However, inventions containing isolated genes which are identical to those found in nature may be patented, provided that the criteria of novelty, inventive step and industrial application are met. In addition, certain processes and things, such as modifying the germ line genetic identity of human beings, cannot be patented because their commercial exploitation would be contrary to the provisions in patent law derived from the EU Directive on biotechnological inventions. This directive was produced to clarify the scope of patenting biological material and to reflect the consensus views about the morality of patents relating to this type of material. The way the UK-IPO examines patent applications relating to biotechnological inventions is set out in guidelines.[10] It should be noted, however, that bioinformatics inventions often comprise software. Patents are not allowed in the UK and Europe for computer programs as such, but inventions making a contribution beyond this can be patented. In contrast, the US does allow patents for computer programs.

Some governments, research institutes and NGOs have raised concerns that the patenting of genetic inventions would lead to excessive prices being charged, particularly for diagnostic tests, and less research being conducted. There have also been some objections to the very notion of patenting genetic inventions per se. The patent system seeks to provide a balance between granting a limited period of exclusivity in order to provide an incentive to innovate, and the wider public interests in providing access to new technologies and technical information. This is particularly appropriate in the area of biomedicine in which it may take many years to develop a marketable technology that offers benefit to patients.

[10] http://www.ipo.gov.uk/biotech.pdf

In response to some of the concerns outlined above, OECD member countries agreed to Guidelines for the Licensing of Genetic Inventions.[11] The UK supported the drafting of these guidelines, which represent best practice, with the aim of promoting innovation and research while maintaining appropriate access to health products and services.

A research report conducted by the Intellectual Property Institute (IPI) in 2004 for the DTI supported the view that the current law and practice in the UK met the needs of researchers.[12] The report also found that there was uncertainty about the scope of the patent research exemption. Such exemptions allow researchers to conduct research on patented inventions without the permission of the patent holder, with the aim of understanding and improving existing products and processes. The purpose of such an exemption is to lower transaction costs, as a large number of patented materials are often required for the experiments. The Gowers Review of Intellectual Property noted concern that follow-on innovation might be stifled by the lack of certainty or by the royalty demands of patent holders.[13] The UK-IPO will shortly publish an issues paper on the current operation of the exemption.

While the Gowers Review highlighted some historical concerns about the patenting of genes, it indicated that current policies for the scope of patents in this area were set at the right level and recommended that these should be maintained.

[11] http://www.oecd.org/dataoecd/39/38/36198812.pdf

[12] *Patents for Genetic Sequences: the competitiveness of current UK law and practice*, http://www.berr.gov.uk/files/file10475.pdf

[13] http://www.hm-treasury.gov.uk/media/6/E/pbr06_gowers_report_755.pdf

Chapter 4: Search Strategy

This chapter explains the search strategy that was adopted to determine the patent landscape for genomic medicine.

It is directed specifically towards answering the questions in the Call for Evidence related to Research & Development (see Annex 1).

Search Strategy

As mentioned in the previous chapter, genomic medicine involves the application of the outcomes of research into genomics to understand and develop treatments for multifactor conditions such as cancer and Alzheimer's disease.

In order to assess the state of development of genomic medicine in the UK, it is necessary to examine the work being carried out within the field of genomics which provide an understanding of the genetic and environmental factors that cause disease in humans and how these factors interact together to exert their effect, what model systems can be used to study how the disease develops and progresses, what model systems can be used to study how these gene-derived conditions can be treated. The latter may involve various models systems in animals or other living organisms as well as the use of computer based modelling techniques to explore mechanisms and pathways of treatment.

For this reason, the search strategy developed looks at a number of different areas of technology which all contribute to the understanding of how genes work simultaneously.

Eight different areas were searched. A brief explanation of each of these areas and the connections between them and their relevance to the field of Genomic medicine is provided below. The terms in **bold** have been used to identify these areas in the Figures, Tables and Graphs in the following Chapters and the Annexes of this report.

The area of **human genes** includes patents relating to isolated forms of human genes and the RNA and protein molecules which they encode, together with their variants and fragments. Knowledge and understanding of the human genome and its encoded proteins and RNA molecules is the basis of genomic medicine. This does not, however, give the complete picture; all cells in the body have the same complement of genes, but the very different characteristics of different cell types are largely a function of the differential regulation of this set of genes, and the mechanisms behind this form the subject matter of the patents for **genes and regulatory sequences**. Aberrant regulation of a gene or genes may be the cause of pathology, or a diagnostic

feature of pathology. Many patents in this area relate to methods of testing the effects of DNA sequences on the expression of genes in their vicinity. Identification of regulatory sequences may help understand the molecular basis of diseases, and is also used to improve the efficiency of recombinant production of commercially and medically important proteins in different host organisms.

The patents falling within the field of **SNPs/haplotypes** are concerned with genetic variation between individuals, and its implications for predisposition, diagnosis, prognosis and treatment of human diseases. *Single nucleotide polymorphisms* (*SNPs*) are single point differences or mutations in the genomic DNA sequence that have been identified between individuals in the human population and a vast number are known. Groups of linked SNPs are known as *haplotypes* – identification of haplotypes can be more technically complex than individual SNPs, but can provide more significant diagnostic information. The identification SNPs, and of correlations (whether causative or otherwise) between SNPs and diseases is a major field of research, which has necessitated the development of research tools (such as microarrays) and associated computer software and hardware to analyse the results. The methods and tools used for investigating SNPs and haplotypes overlap with the technology used to investigate **gene expression profiles**. Gene expression analysis measures quantitative differences in gene expression, by determining the presence or quantity of RNA or protein molecules encoded by the genes in question. The detection of alterations in gene expression (whether of a single gene or many genes) is a very important diagnostic tool, particularly in the detection and characterisation of cancers.

Proteins are responsible for catalysing most of the chemical reactions in the body, and transmitting and receiving signals between cells. As such, they are the target molecules for most pharmaceuticals, and so understanding of **protein structure** is critical for understanding the basis of their function, and developing pharmaceuticals which modulate, enhance or inhibit their activity as required. Methods of analysing protein structure include *in vitro* crystallisation and crystallography, and *in silico* computer modelling. Cellular proteins do not act in isolation, and so the study of **protein-protein interactions** is critical for understanding the molecular basis of diseases and the possible therapeutic targets. Such interactions include the interactions between circulating hormones and the cell-surface receptors that bind them, and between the receptors and the proteins within the cell that transmit and affect the cell's response to the hormonal signal.

The final two areas both relate to developments in the tools available for research in genomic medicine. Genetically **modified animals** have been produced to investigate mammalian development, to provide models for human diseases, and to screen and test potential therapies and/or environmental hazards. The development of **algorithms and software** has been an essential tool in identifying and characterising the vast amount of sequence and other biological data, interpreting gene expression or mutation profiles, and modelling the structures of biological molecules.

A similar strategy was adopted by the US National Academy of Sciences in its recent study on Genomics and its implications for Public Health.[14]

The searches were performed by identifying the relevant classification terms used in the ECLA and IPC classification systems for patent applications to denote features in an area of technology relevant to Genomic Medicine. These were searched in combination with a number of key words and expressions. Relevant abbreviations, alternative names or synonyms were also included in each search. The searches were carried out in the EPOQUE database at the UK-IPO.

[14] "Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health", report by the Committee on Intellectual Property Rights in Genomic and Protein Research and Innovation, National Research Council, US national Academy of Science, pp 100-132 and pp 169-171 (appendix B), available from http://www.nap.edu/openbook.php?record_id=11487&page=100 [accessed 20 Mar 2008]

Chapter 5: What is the state of the science? What new developments are there? What is the rate of change?

Research and Development in the area of biotechnology has grown rapidly in the last 20 years and remains very active. Patents are a useful indicator of innovative activity and there is a wealth of patent information on biotechnology.

The numbers of patents for inventions in the general field of Biotechnology which includes Genomics and Genomic Medicine represent a significant portion of the overall numbers of patents applied for in the last 20 years. In the period 1985-2000, the numbers of biotechnological patents have increased both in numeric terms and as a portion of the overall numbers of patents applied for as indicated in **Figure 5.1**. Making allowance for the fact that the figures from 2005-2006 are incomplete[15], it is clear there has been a decline in the numbers of patents for biotechnological inventions since 2000 while the overall numbers of patent applied for have remained steady.

The overall trend that can be observed includes an increasingly rapid rise in patent applications from the technology's infancy in the early eighties to a peak in around 1999-2002. Since then there has been a pronounced down-turn in the total volume of patent applications in this field (even allowing for the artefacts of the method referred to above).

This down-turn may have several causes; firstly there was a "biotechnology bubble", and the after-effects of this may have led to more cautious investment and patent filing strategies. Secondly, changes in practice by patent offices worldwide may have led to a reduction in speculative patent filings, particularly relating to gene and protein sequences. Patents are granted for inventions that are new, inventive and capable of industrial application. The criteria used by patent offices to determine inventiveness and industrial applicability (utility) of newly isolated DNA or protein sequences have generally become stricter – in particular, most major patent offices would now require that a patent application discloses the function of a new gene sequence.

[15] The data are based on the priority year of the invention, that is year which best reflects when an invention was made. It should be noted that patent applications are not usually published until 18 months after this priority date. In addition, the data is based on the ECLA classification applied by the European Patent Office - there is often a time-lag of up to a year before the ECLA mark is applied. The effect of this is that the sharp apparent fall in applications from 2005 onwards may in part an artefact of the data collection method.

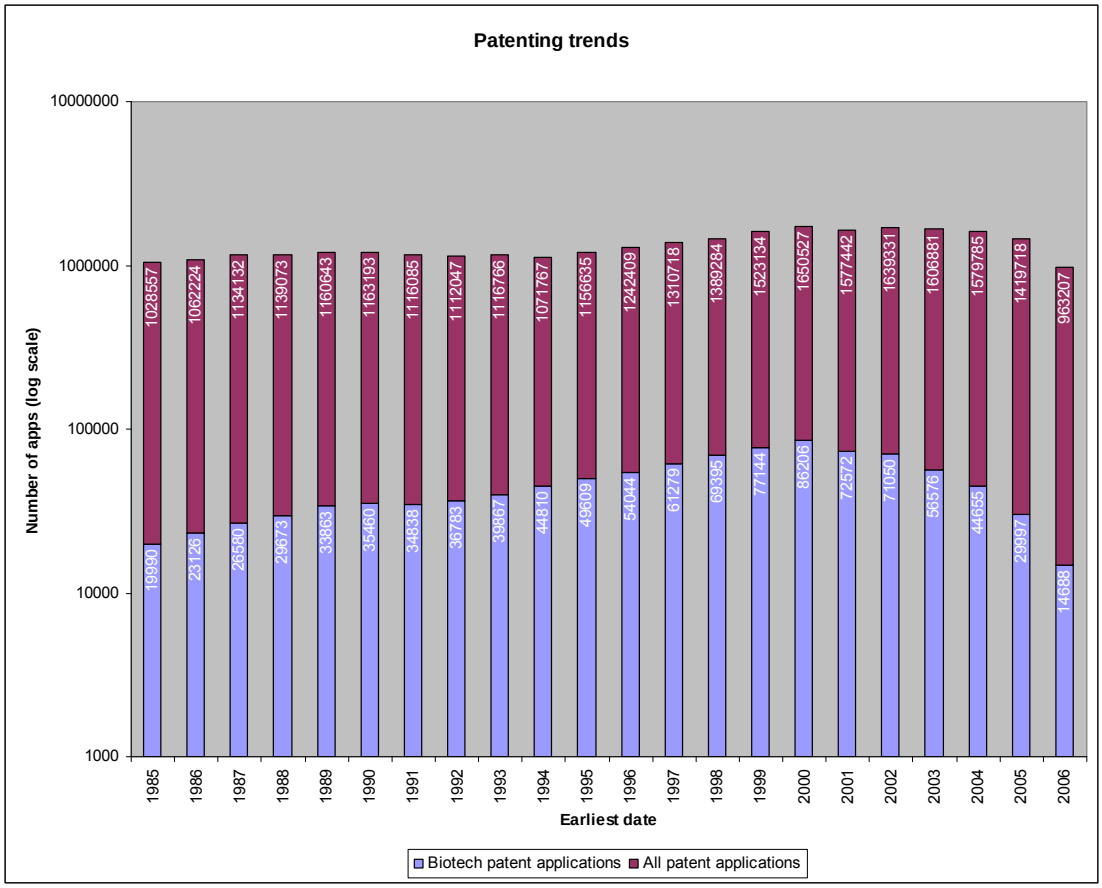

Figure 5.1. Patent applications in all areas compared to those in biotechnology for period 1985-2006 (see footnote [16])

The eight technology areas relevant to Genomic Medicine all echo this trend as shown in **Figure 5.2**. The down turn is most noticeable in relation to patents for new **human genes**. As can be seen from **Figure 5.2**, patent filings in this area peaked earlier than in other fields (2000) and have rapidly declined since. This reflects in part the reasons mentioned above, and in part a specific technical reason. The rapid rise in patent applications for **human genes** reflects the explosion in human gene discovery in the years leading up to the full sequencing of the human genome, completed in 2002. Since 2000, the rapid fall in new human gene patents reflects the fact that it is unlikely that there are significant numbers of human genes still to be identified. Patent activity in the field has instead increasingly focussed on the diagnostic uses of genetic information (e.g., from **SNP/haplotypes** data and **gene expression profiles**), the analysis of how genes and proteins interact with each other (i.e., genomics and proteomics[17]), and the use of transgenic animals as model systems.

[16] Patent applications filed by earliest priority date, in all subjects vs Biotech (IPC classification marks A01K 67/027, A61K 38/, 38/, 48/, C07K, C12N 9/, 15/, C12Q, G01N 33/48 - 33/98, C40B)

[17] **Proteomics** is the large-scale study of proteins, particularly their structures and functions. The term "proteomics" was coined to make an analogy with genomics, the study of the genes. The word "**proteome**" is a blend of "**protein**" and "**genome**". The **proteome** is the entire complement of proteins produced by an organism or system. This will vary with time.

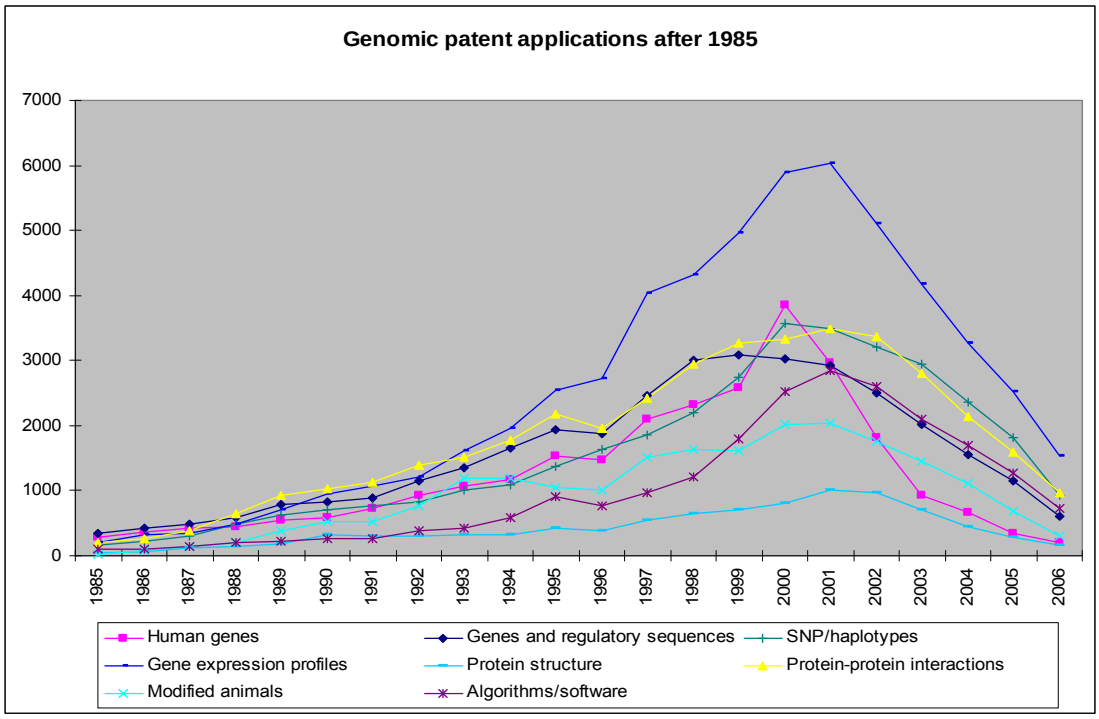

Figure 5.2 Overview of genomic patent applications after 1985

Most Cited Patents

To gain an insight into the state of the science, it is helpful to consider what kind of technology is being used most widely within the research area of interest. **Table 5.1** lists the most frequently cited patent documents among patents in each of the 8 areas of technology relevant to Genomic Medicine.

For each subject area the most frequently cited patent is shown, and the most frequently cited patent with a UK inventor or applicant. It should be noted that several of these patents lead the citation lists in several different subject areas, emphasising the inter-dependence of research across these fields.

For example, US4683195 (CETUS) is the most-cited patent in the field of human genes, SNP/haplotypes and gene expression profiles, while the closely related patent US4683202 (CETUS) is the most cited patent in the

---

Proteomics is often considered the next step in the study of biological systems, after genomics. It is much more complicated than genomics, mostly because while an organism's genome is rather constant, a **proteome** differs from cell to cell and constantly changes through its biochemical interactions with the genome and the environment. One organism has radically different protein expression in different parts of its body, different stages of its life cycle and different environmental conditions. Another major difficulty is the complexity of proteins relative to nucleic acids. E.g., in humans there are about 25 000 identified genes but an estimated >500 000 proteins that are derived from these genes. This increased complexity derives from mechanisms such as alternative splicing, protein modification (glycosylation,phosphorylation) and protein degradation.

field of algorithms and software. These two related patents both relate to the original invention of the polymerase chain reaction (PCR). This is a method for amplifying specific sequences or regions of DNA, and lies at the heart of most modern techniques for analysing, detecting and manipulating DNA and RNA sequences. The leading citation for both genes and regulatory sequences, and protein-protein interactions, relates to the yeast “two-hybrid” system. This is a method of detecting protein interactions, using reporter genes to provide a detectable gene product when two proteins interact, and so utilises gene expression technology to study protein-protein interactions. The leading citation for protein structure patents is a patent which describes a computer based system to design recombinant proteins which can mimic the specific binding activity of an antibody. Finally, the leading citation for modified animals is US4736866 (HARVARD), the “Harvard Oncomouse”, which is a mouse genetically modified to be susceptible to cancer. These patents indicate that the most significant patents in terms of long-term impact in the field tend to be those that introduce new research tools or methods, rather than new discoveries of biological phenomena

The most significant patents with a UK inventor and/or applicant are also listed, and again several of these are cited across different disciplines. The leading UK citation for SNP/haplotypes, gene expression profiles and algorithms and software is WO89/10977 (ISIS INNOVATIONS/SOUTHERN), which relates to an array of nucleic acid probes for detecting multiple sequences. Such arrays are very widely used for both SNP detection and gene expression profiling, and they often require sophisticated computer based analyses to interpret the results. EP0239400 (MRC/WINTER) is a method of making recombinant antibodies where the binding specificity is manipulated by mutating particular regions of the antibody gene – this is significant both for the structure of the antibody itself and its binding to its target antigen, and so is heavily cited in both the protein structure and protein-protein interaction fields.

WO02/04520 (INCYTE/HARLAND ET AL) describes the cloning and sequencing of 32 cell membrane proteins, and is typical of the gene discovery patent applications that were filed in very large numbers as the human genome project neared completion (the original priority date was 2000 – the peak year for this type of patent application). This is the leading citation with a UK inventor (working in collaboration with a US team) in the field of human genes. WO90/08830 (ICI/BRIGHT ET AL) – heavily cited in the field of genes and regulatory sequences – is a method of plant genetic modification. Finally WO88/00239 (PHARMACEUTICAL PROTEINS/CLARK ET AL) is a method of producing large quantities of useful proteins by expressing them under the control of a DNA element which causes the protein to be secreted into the milk of a recombinant sheep, potentially raising the possibility of “biopharming”.

Table 5.1 The most cited patent in each of the eight areas of technology relevant to Genomic Medicine

Subject area	Most cited patent documents				
	Worldwide		With UK applicant or inventor		
	Document	No. citations	Document	No. citations	Details
Human genes	US4683195 (CETUS)	55	WO0204520 (position 70)	14	Harland (GB) working at Incyte Genomics (US)
Genes and regulatory sequences	US5283173 (UNIV NY)	63	WO9008830 (position 10)	25	Bright (GB), Greenland (GB), Schuch (GB), Bridges (US) working at ICI (GB)
SNP/haplotypes	US4683195 (CETUS)	184	WO8910977 (position 23)	47	Southern (GB) working at Isis Innovations (GB)
Gene expression profiles	US4683195 (CETUS)	262	WO8910977 (position 7)	67	Southern (GB) working at Isis Innovations (GB)
Protein structure	US4704692 (GENUX)	21	EP0239400 (position 12)	13	Winter (GB) working at Medical Research Council (GB)
Protein-protein interactions	US5283173 (UNIV NY)	61	EP0239400 (position 4)	45	Winter (GB) working at Medical Research Council (GB)
Modified animals	US4736866 (HARVARD)	78	WO8800239 (position 4)	37	Clark (GB) and Lathe (FR) working at Pharmaceutical Proteins (GB)
Algorithms/software	US4683202 (CETUS)	40	WO8910977 (position 13)	18	Southern (GB) working at Isis Innovations (GB)

Chapter 6: Who is taking the lead in the consideration and co-ordination of research and the development of new technologies?

By looking at the top 25 patent applicants in an area of technology, it is possible to gain an insight into who the leading players are in this technology.

Figures 6.1 to 6.8 show the Top 25 patent applicants in each of the eight technology areas relevant to Genomic Medicine. **Figures 6.1-6.3** are included below as examples and **Figures 6.4-6.8** are included in the Annex to Chapter 6. Applicants identified by a red bar are UK companies or those with a significant UK research & development operation, UK universities or UK research charities or public sector research institutes.

The eight technology areas relevant to Genomic Medicine can be ranked as shown in **Table 6.1** on the basis of patents filed.

Table 6.1: Ranking in terms of patent activity of the eight technology areas relevant to Genomic Medicine

Patent Activity Ranking*	Area	Figure£
1	Gene expression profiles	6.1
2	Human genes	6.2
=3	Genes and regulatory sequences	6.3
=3	Protein-protein interactions	6.4
5	SNP/haplotypes	6.5
6	Algorithms/software	6.6
7	Modified animals	6.7
8	Protein structure	6.8

*measured in terms of patent applications filed

£Figures 6.4 to 6.8 are in Annex to Chapter 6

It is clear from a consideration of **Figures 6.1 to 6.8** that Genomic Medicine is an area of interest that is attracting significant interest worldwide. The leading pharmaceutical companies from US, Europe (Germany, France, UK and Switzerland) and Japan are all involved to a significant degree in all the relevant areas of research. This wide and significant level of interest is not surprising given that a greater understanding of how genes and proteins interact together and with each other is essential to the understanding of disease and the development of future therapies. Future treatments are likely to be much more personalised or tailored to the patient's genome in order to be effective and reduce side effects.

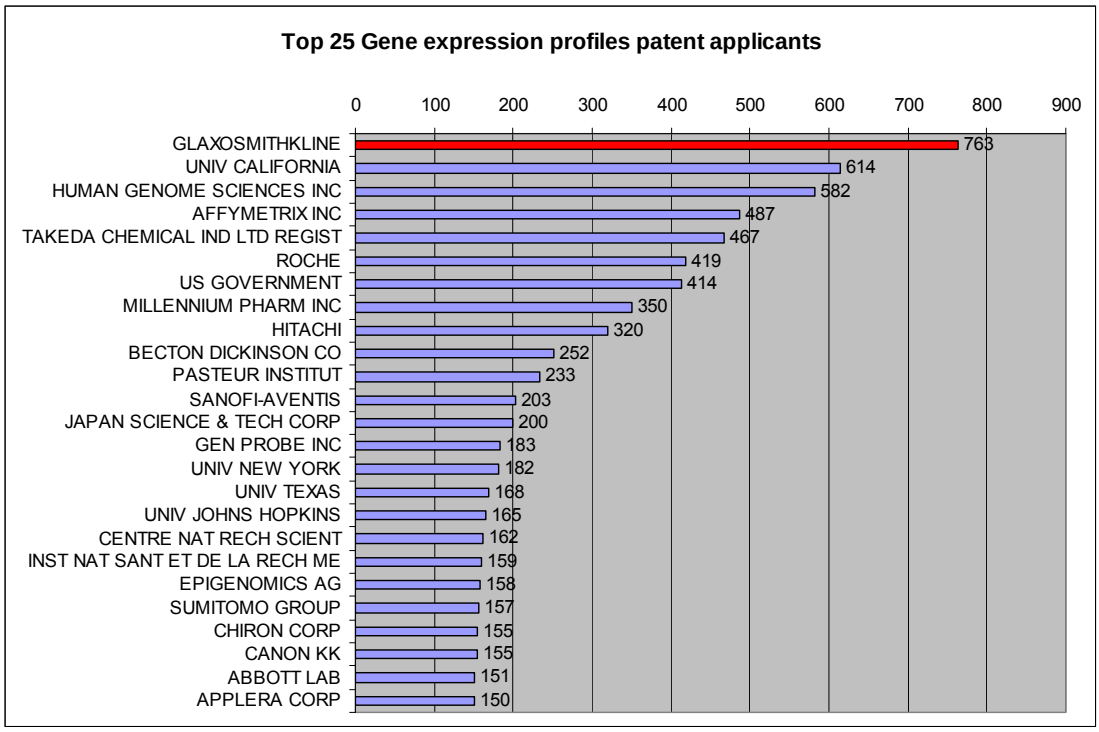

Figure 6.1 Top 25 applicants in the field of **gene expression profiles**

The greatest activity in relation to Genomic Medicine is taking place in the US. A significant number of the top 25 applicants in each area are US based and include large US pharmaceutical companies, specialist biotechnology companies, universities and research institutes. In general the majority of applicants in the top 25 in each area are from the corporate sector and are US companies.

In addition to US industry taking a significant interest in the research in all areas that are relevant to Genomic Medicine, the US Government is also a significant patent applicant in each of these eight areas. The leading academic sector applicant in all eight areas of technology is also based in the US, the University of California. This is pointing to a significant investment of public and private funds in Genomics and Genomic Medicine in the US to develop a significant research capacity in these areas and, in turn, to lay the foundation for a significant commercial sector.

However, significant representation in the top 25 across all areas is found for applicants from Japan, France, & UK. In only one area, was a significant Chinese presence noted, a specialist biotechnological company, Shanghai BioWindow Gene Development is ranked 4th in the area of **human gene patents** (see **Figure 6.2**).

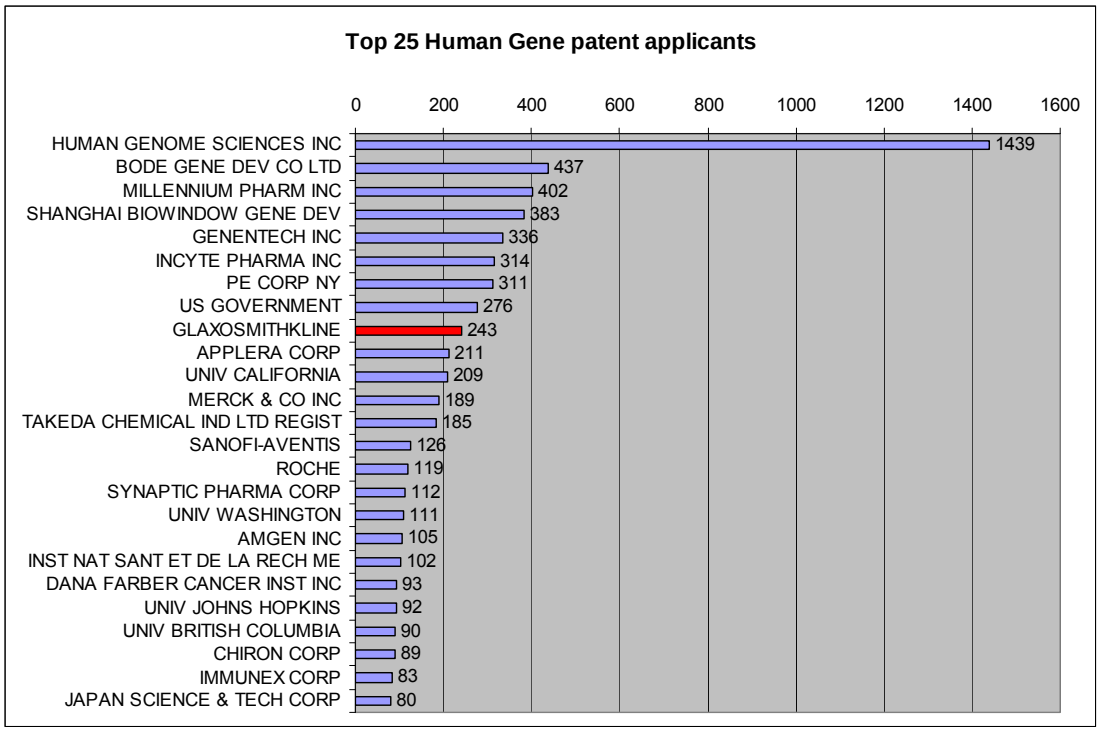

Figure 6.2 Top 25 applicants in the field of **human genes**

As indicated in Table 1, the greatest degree of patent activity in areas relevant to Genomic medicine, in terms of patents applied for are in **gene expression profile patents** (see **Figure 6.1**) and **human gene patents** (see **Figure 6.2**). The 25 leading applicants for **gene expression profile patents** are heavily involved in this area with the top 5 ranked applicants having a very similar numbers of patents (see **Figure 6.1**). By contrast the top ranked applicant in the area of **human genes** has over 3 times as many as the 2nd ranked (see **Figure 6.2**, 1439 patent applications v 437 patent applications) and each of the other applicants ranked in the top 25 has significantly fewer patent applications than the correspondingly ranked applicant in the area of **gene expression profile patents** (see **Figure 6.1**)**.**

The leading players, especially the top 6, in the area of **human gene patents** are specialist biotechnology companies – the leading pharmaceutical applicant in this area is UK/US multinational pharmaceutical company GlaxoSmithKline, in 9th place (see **Figure 6.2**).

The other area where there appears to be a significant number of specialist companies involved is that of **gene-related algorithms/software.** As well as specialist biotechnology companies who have developed bioinformatics databases and techniques (e.g., Human Genome Sciences Inc, from the US, ranked 1st), the leading electronics companies from the US, Europe and Japan are amongst the top 25 applicants in this area (see **Figure 6.**6 in Annex to Chapter 6)**.**

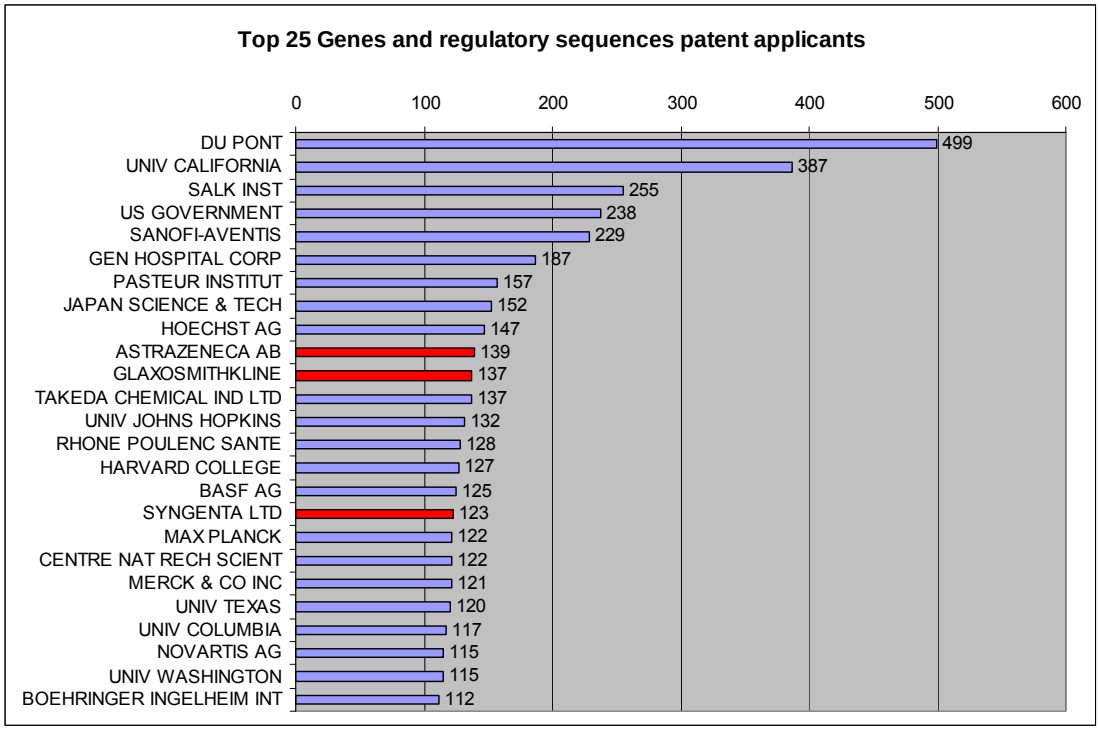

Figure 6.3 Top 25 applicants in the field of **genes and regulatory sequences**

In contrast, the applicants in the area of **gene expression profile patents** represent a greater cross section of big pharmaceutical companies, smaller biotechnology and specialised companies and universities or other public research bodies. The leading player in this area is the large UK/US pharmaceutical company GlaxoSmithKline (see **Figure 6.1**). This more diverse mixture of Top 25 applicants is also seen in the areas of technology covered in **Figures 6.4-6.8** (see Annex to Chapter 6).

It is only in the area of **modified animal patents** that there are more academic/research sector applicants that corporate sector applicants (see **Figure 6.7**). This may indicate that this technology is still primarily directed towards providing tools for basic research, for example by developing model systems in animals with or without specific genes in order to study the effects of such changes.. Again the majority of these academic/research sector applicants are US based. However, there are also academic/research sector applicants who are based in Japan & Europe in the top 25. There are 4 academic/research sector applicants based in France in the top 25 (ranked 5th, 12th 18th, 25th) and one corporate sector applicant (ranked 22nd). The leading UK applicant is this area is the Medical Research Council, ranked 6th overall.

It is noticeable that UK based applicants are significant players in all eight areas of technology.

Two large pharmaceutical companies with significant UK based operations, US/UK multinational GlaxoSmithKline and UK/Swedish multinational

AstraZeneca are active in all eight areas of technology of relevance to Genomic Medicine. Indeed GlaxoSmithKline is the leading applicant in the area of **gene expression profile patents** (see **Figure 6.2**) and is ranked 2nd in **gene-related algorithms/software** (see **Figure 6.7**). Other UK companies active in some of these areas include *SYNGENTA*, ranked 17th, in the area of **genes and regulatory sequences patents** (see **Figure 6.3**)**; and** *ICI*, ranked 14th in the area of **SNP/haplotype patents**(see **Figure 6.4**)**.**

The only UK based academic/research sector applicant making the top 25 is the Medical Research Council, ranked 5th in **modified animal patents** (see **Figure 6.7**) and 25th in **protein structure patents** (see **Figure 6.8**)**.**

The other European country, in addition to the UK, that has a significant representation in terms of both corporate and research/academic applicants in the top 25 is France. French based academic/research sector applicants are active in 6 of the 8 areas relevant to Genomic Medicine as is one French based corporate applicant (Sanofi-Aventis). While pharmaceutical companies with significant operations in other European countries (Germany, Switzerland and Norway) such as Roche, Novartis AG, Bayer AG, NovoNordisk AS and Hoescht AG are involved in research relevant to Genomic Medicine, no academic/research sector applicants from these countries has made the top 25 in these areas (see **Figures 6.1 to 6.8**).

Chapter 7: How does research in the UK compare internationally? How much collaboration is there Introduction?

Following on from Chapter 6, we can look in more detail at the distribution of the type of applicant for patents in the eight areas of relevance to Genomic Medicine.

Figures 7.1-7.8 below show the distribution of patents applied for by sector, i.e., corporate, academic, government or hospital, for each of the areas of interest, both worldwide and for UK only.

Comparing the UK pattern of patent filings with the worldwide pattern for all eights areas of technology relevant to Genomic Medicine, there are two significant differences. Firstly, the academic sector in the UK is very strong and contributes a higher proportion of patent filings than in the rest of the world, in virtually all the subject areas examined.

Secondly, there appears to be very little patent filing activity from the hospital sector in the UK, whereas worldwide this is a minor, but still significant contribution to the total. Given the importance of clinical research in developing and understanding disease conditions, it would be worth considering why this situation arises. In the UK many hospitals, including all the major teaching hospitals, are closely linked to a university medical school. As a result, patents arising from research work carried out in the hospital environment and involving both clinical and academic researchers may be assigned to the University rather than the Hospital Trust. Also, it is only recently that the UK National Health System has put in place a policy framework and system for dealing with patents and other forms of IP. However, It is noticeable that 2 UK Hospital trusts have begun to file patent applications in two areas of technology, (see entries 25 and 29 in **Table 7.2** for Tayside University Hospitals and St James & Seacroft University Hospitals respectivity.)

Table 7.1 lists all the UK-based corporate entities that have applied for patents in the eight areas of technology relevant to Genomic Medicine. **Table 7.2** lists the corresponding UK-based universities and **Table 7.3** lists the corresponding UK-based public research bodies/research institutes. These tables provide a clear illustration of the breadth and diversity of UK based research activity in Genomic Medicine. Of the 161 UK entities identified, 116 are companies, 29 are universities and 16 are public research bodies/ charities

As the same patent may be included in more than one area given the degree of interdependence of these areas of technology, the numbers of patents are

indicative of each entities interest in these areas rather than an accurate picture of the total number of UK patent filings per entity in each subject[18].

In addition to the UK universities that are active in Genomic Medicine, the commercial sector in the UK includes a number of highly active university spin-out companies, such as Isis Innovation and Imperial College Innovations Limited, as well as a spin-out company formed by the John Innes Centre a public sector research institute in the fields of agriculture and food. These companies are actively involved in the transfer of technology and skills from the academic/public research sector to the commercial sector through licensing, spin-outs and consulting.

Table 7.1 also shows that two UK hospital trusts, Tayside Universities Hospitals and St James & Seacroft University Hospitals have begun to file patents in the area of **gene expression profiles** and **SNP/haplotypes** respectively.

Having identified all the UK companies, universities and public bodies/charities involved in genomic medicine related areas of technology, it is possible to map the degree to which these entities have been involved in collaborating with other companies, universities and public bodies/charities.

A collaboration map for each area of technology as indicated in below is shown in the Annex to Chapter 7 (see **Figures 7.9** to **7.16**)..

Collaboration Map	Figure (in Annex)
Human gene patents	**7.9**
Protein structure patents	**7.10**
Gene expression profile patents	**7.11**
Genes and regulatory sequences	**7.12**
Protein-protein interactions	**7.13**
SNP/haplotypes	**7.14**
Algorithms/software	**7.15**
Modified animals	**7.16**

The general conclusion from a consideration of all eight collaboration maps is that UK entities are involved in a large number of collaborations both within the UK and abroad. These collaborations involve UK entities working with many of the top corporate and academic/public research entities in each area of technology of relevance to Genomic Medicine as identified in Chapter 6 (see **Figures 6.1-6.8**) . These collaborations involve a good cross section of UK entities – large pharmaceutical companies, smaller specialised biotechnology companies, universities, research charities and public bodies.

[18] for further explanation, see footnote 20.

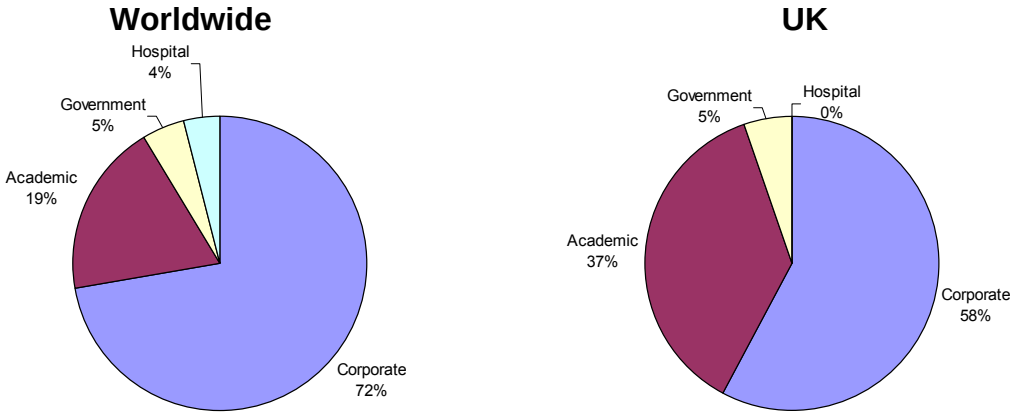

Figure 7.1 Distribution of **human gene patent** applications

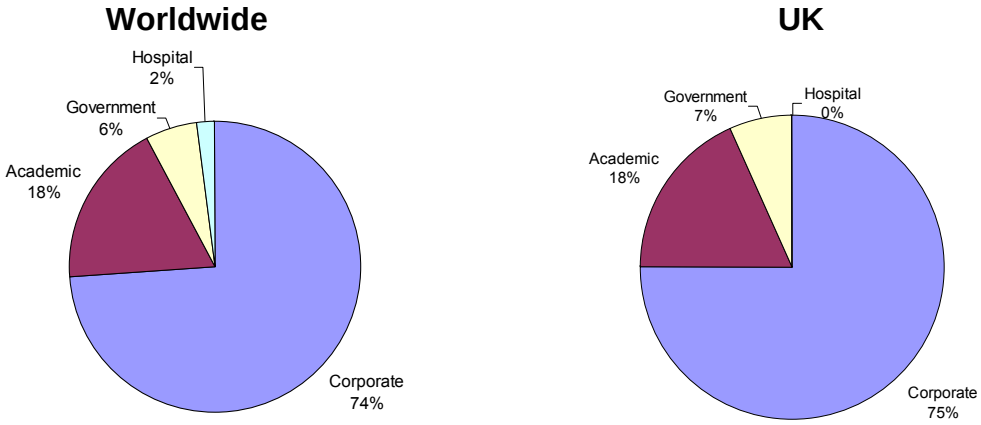

Figure 7.2 Distribution of **genes and regulatory sequences** patent applications

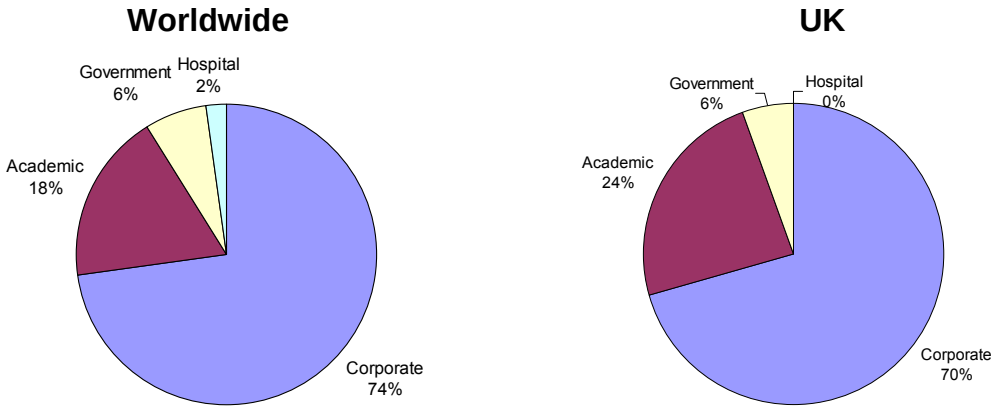

Figure 7.3 Distribution of **SNP/haplotypes** patent applications

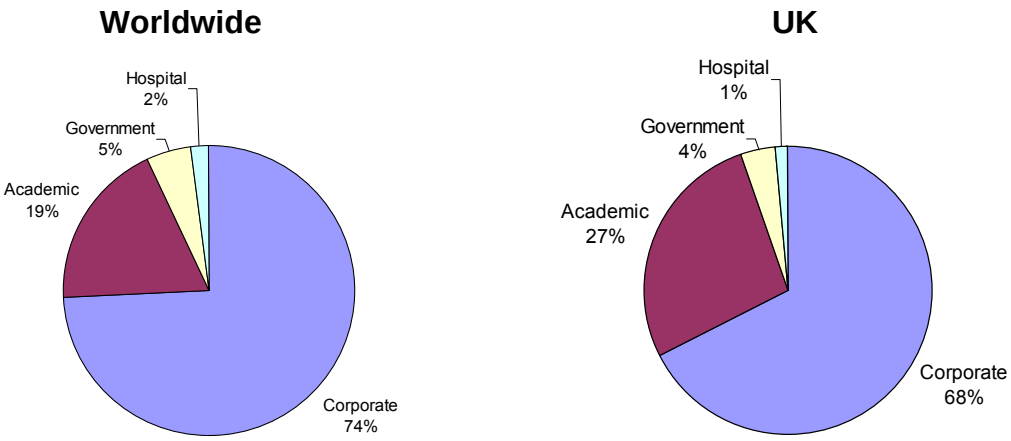

Figure 7.4 Distribution of **gene expression profiles** patent applications

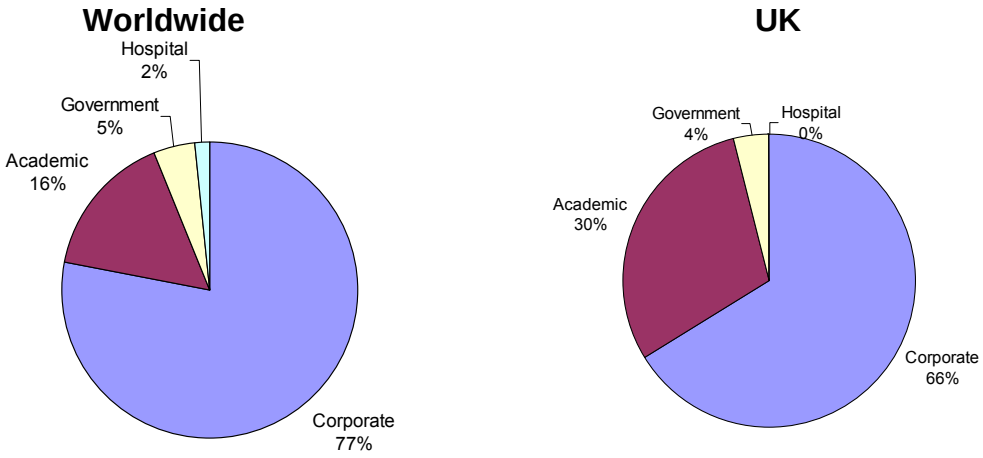

Figure 7.5 Distribution of **protein structure** patent applications

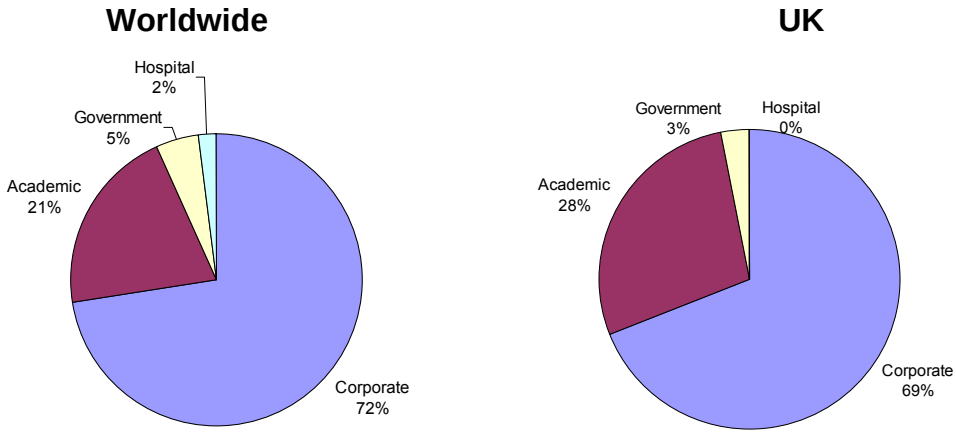

Figure 7.6 Distribution of **protein-protein interactions** patent applications

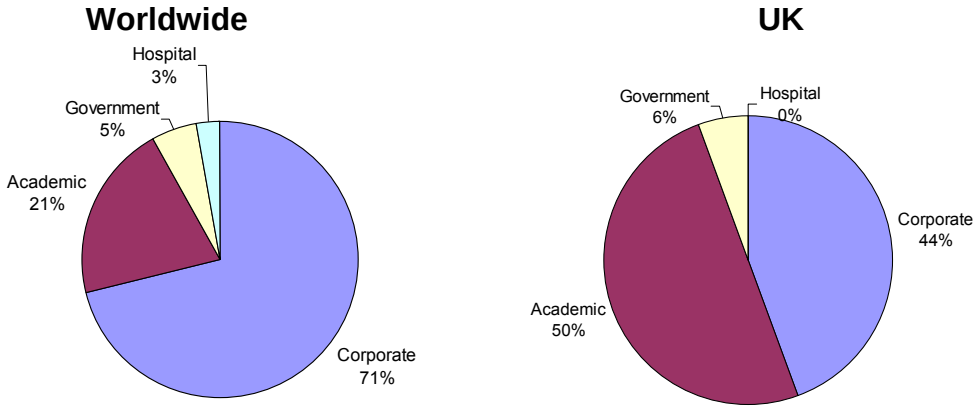

Figure 7.7 Distribution of **modified animals** patent applications

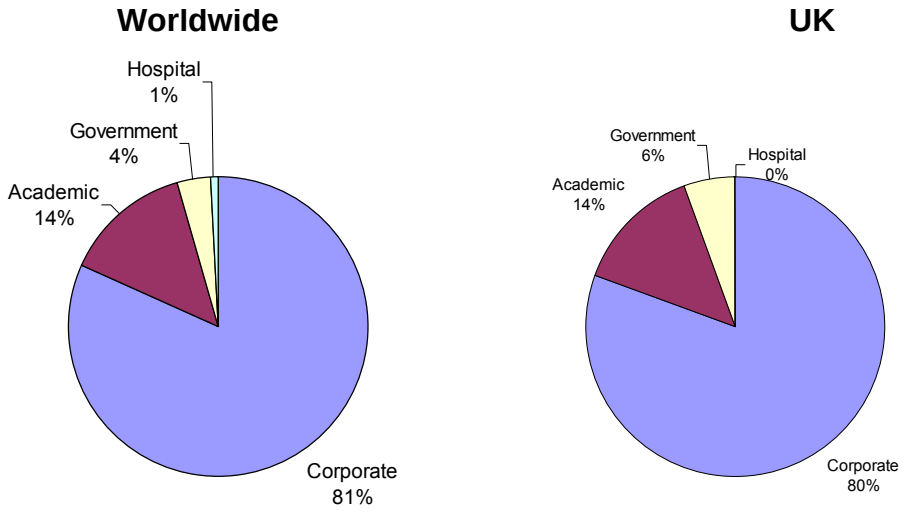

Figure 7.8 Distribution of **gene related algorithms/software** patent applications

Table 7.1: UK companies that have applied for patents in the eight areas of technology relevant to Genomic medicine.

Top UK companies		Human genes	Genes and regulatory sequences	SNP/haplotypes	Gene expression profiles	Protein structure	Protein-protein interactions	Modified animals	Algorithms/software
1.	GLAXOSMITHKLINE	243	137	173	760	38	150	33	194
2.	ASTRAZENECA AB		139	188	89	53	76	60	
3.	SYNGENTA		123	31	55	4			5
4.	ICI PLC		33	145	23		13		3
5.	ISIS INNOVATION	11		67	36	6	22	11	16
6.	APPLIED RESEARCH SYSTEMS		20	14	7		65		42
7.	UNILEVER PLC		23	20	3	20	70		7
8.	CELLTECH LTD	8	24	4	11		81		
9.	VISIBLE GENETICS INC			65	36		3		16
10.	INPHARMATICA LTD					37	37		13
11.	CYTOKINETICS INC				80				6
12.	CAMBRIDGE ADVANCED TECH		73			5			7
13.	AFFYMAX TECH NV		6	15	42		16		4
14.	IMP COLLEGE INNOVATIONS LTD		17	6	4	6	17	28	
15.	BTG INT LTD	4	32		9	3	27		
16.	CAMBRIDGE ANTIBODY TECH				8	11	47		4
17.	PLANT BIOSCIENCE LTD		28	28			8		
18.	DOMANTIS LTD		8			6	42		
19.	IMUTRAN LTD	16					10	30	
20.	ASTERION LTD					17	20		
21.	OXFORD BIOMEDICA LTD		35						
22.	OXFORD GENE TECH LTD			18	17				
23.	CYCLACEL LTD		7				19	4	
24.	APPLIED GENE TECHNOLOGIES INC		7	4	11		5		
25.	ASTEX TECHNOLOGY LTD					19			6
26.	GENDAQ LTD		7		5	3	4		3
27.	SEQUENOM GEMINI LIMTED			13	7				
28.	DYNAL BIOTECH LLC			15	4				
29.	SCIENT GENERICS LTD		5		10				3
30.	FORENSIC SCIENCE SERVICE LTD			8					9
31.	SOLEXA LTD				13				4
32.	ACCENTUS PLC					16			
33.	DELTA BIOTECHNOLOGY LTD	6	13				3		
34.	GEMINI GENOMICS PLC			13	3				
35.	INNES JOHN CENTRE INNOV LTD		4	12					
36.	KUDOS PHARM LTD	3			10		6		
37.	OXFORD GLYCOSCIENCES UK LTD				7		3		6
38.	PROLIFIX LTD		6			4	6		
39.	SENSE PROTEOMIC LTD			6	7		3		
40.	AGRICULTURAL GENETICS CO		15						
41.	GEMINI RES LTD			15					

Top UK companies (cont'd)

		Human genes	Genes and regulatory sequences	SNP/haplotypes	Gene expression profiles	Protein structure	Protein-protein interactions	Modified animals	Algorithms/software
42.	SCIONA LTD			8					7
43.	CIPLA LTD			14					
44.	MEDICAL BIOSYSTEMS LTD			9	5				
45.	BIOGEMMA UK LTD		13						
46.	BIOTICA TECH LTD		5	4	3				
47.	GENTRONIX LTD		8		4				
48.	PROTEOM LTD								12
49.	RIBOTARGETS LTD				7		4		
50.	BIO GENE LIMITED			4	6				
51.	BRITISH TELECOMM								10
52.	MOLECULAR LIGHT TECH RES LTD		6		4				
53.	POWDERJECT RES LTD		10						
54.	SHELL INT RESEARCH		10						
55.	ANTISOMA PLC			4			5		
56.	RENOVO LTD			9					
57.	ACTINOVA LTD		3				5		
58.	AVIDEX LTD				4		4		
59.	BIOTAL LTD		8						
60.	BP NUTRITION		8						
61.	BRAX GROUP LTD			4	4				
62.	COGENT LTD				8				
63.	GENOSTIC PHARMA LTD			8					
64.	HEXAGEN TECHNOLOGY LIMITED			8					
65.	OXAGEN LTD			8					
66.	PIG IMPROVEMENT COMPANY UK LTD			8					
67.	SCHERING AGROCHEMICALS LTD		8						
68.	TEPNEL MEDICAL LTD			5	3				
69.	ENIGMA DIAGNOSTICS LTD			4	3				
70.	HEALTH LAB SERVICE BOARD		7						
71.	NICKERSON BIOCEM LTD		7						
72.	TCS CELLWORKS LTD		3	4					
73.	TRANSITIVE LTD			7					
74.	ADVANCED RISC MACH LTD								6
75.	BIOVEX LTD		6						
76.	BRAX GENOMICS LTD			3	3				
77.	COBRA THERAPEUTICS LTD		3						3
78.	CRUSADE LAB LTD					3	3		
79.	EVOLVA LTD		6						
80.	GYRE LTD					3	3		
81.	ZORAGEN INC				6				
82.	BIOQUANT LTD			5					
83.	EXPRESSON BIOSYSTEMS LTD				5				
84.	3I RES EXPL LTD				4				
85.	ARROW THERAPEUTICS LTD				4				

Top UK companies (cont'd)

		Human genes	Genes and regulatory sequences	SNP/haplotypes	Gene expression profiles	Protein structure	Protein-protein interactions	Modified animals	Algorithms/software
86.	BRITISH BIO TECHNOLOGY	15					4		
87.	CYTOGENETIC DNA SERVICES LTD			4					
88.	DALGETY PLC LONDON			4					
89.	DIATECH LTD		4						
90.	GILTECH LTD								4
91.	LEIV EIRIKSSON NYFOTEK AS		4						
92.	LILLY INDUSTRIES LTD			4					
93.	ML LAB PLC		4						
94.	MOLECULAR SENSORS LTD								4
95.	PHOGEN LTD				4				
96.	PIC FYFIELD LTD			4					
97.	RANDOX LAB LTD				4				
98.	ZENCO NO 4 LTD			4					
99.	ADVANTA TECH LTD		3						
100.	AGREVO UK LTD		3						
101.	ASTEX THERAPEUTICS LTD					3			
102.	BIOINNOVATION LTD		3						
103.	BRITISH PETROLEUM CO PLC			3					
104.	CAMBRIDGE BIOTECH CORP		3						
105.	CAMBRIDGE MOLECULAR TECH								3
106.	CANTAB PHARMA RES		3						
107.	DYNAMETRIX LTD			3					
108.	MARCONI UK INTELLECTUAL PROP								3
109.	MICROBIAL TECHNICS LIMITED				3				
110.	MICROSCIENCE LTD		3						
111.	MONSANTO UK LTD		3						
112.	NICKERSON INT SEED		3						
113.	NONLINEAR DYNAMICS LTD								3
114.	PHOTO THERAPEUTICS LTD				3				
115.	SEPTEGEN LTD		3						
116.	DARWIN DISCOVERY LTD	8							

Table 7.2: UK universities that have applied for patents in the eight areas of technology relevant to Genomic medicine.

Top UK universities	Human genes	Genes and regulatory sequences	SNP/haplotypes	Gene expression profiles	Protein structure	Protein-protein interactions	Modified animals	Algorithms/software
1. ISIS INNOVATION	11		67	36	6	22	11	16
2. UNIV CAMBRIDGE TECH	4	16	10	15	12	14	8	4
3. IMP COLLEGE INNOVATIONS LTD		17	6	4	6	17	28	
4. UNIV WALES		25	10	18			7	3
5. UNIV EDINBURGH	3	3	5	10		5	29	5
6. UNIV DUNDEE	3	15		7	3	21	9	
7. UNIV LONDON	3	15	9	11		9	9	
8. UNIV BRISTOL			10	6	9	9	5	
9. IMPERIAL COLLEGE	3	3	4			4	27	
10. UNIV MANCHESTER	3	11	7	7		7		
11. UNIV GLASGOW		9		9	3	8		
12. UNIV CARDIFF		5	16	7				
13. UNIV ABERDEEN			8	3	3	9	3	
14. UNIV SHEFFIELD	8		11	8				3
15. TRINITY COLLEGE DUBLIN			9			9		
16. UNIV STRATHCLYDE				11	4	3		
17. UNIV LEEDS		7		10				
18. UNIV NOTTINGHAM				8	3	5		
19. UNIV LEICESTER		3	5	4				
20. UNIV BATH					6	5		
21. UNIV BUCKINGHAM		11						
22. UNIV CRANFIELD				6				5
23. UNIV BELFAST				4		4		
24. UNIV PORTSMOUTH				3		3		
25. TAYSIDE UNIVERSITY HOSPITALS				4				
26. UNIV WARWICK		4						
27. BIRKBECK COLLEGE			3					
28. KINGS COLLEGE LONDON			3					
29. ST JAMES AND SEACROFT UNIVERSITY TRUST			3					

Table 7.3: UK public bodies/research institutes that have applied for patents in the eight areas of technology relevant to Genomic medicine.

Top UK public bodies/ research institutes	Human genes	Genes and regulatory sequences	SNP/haplotypes	Gene expression profiles	Protein structure	Protein-protein interactions	Modified animals	Algorithms/software
1. MEDICAL RES COUNCIL	23	71	57	66	31	78	114	31
2. UNITED KINGDOM GOVERNMENT		19	24	80	3	14		11
3. CANCER RESEARCH UK	32	31	46	23	7	30	52	4
4. NAT RES DEV		7					11	
5. HEALTH PROT AGENCY			4	8		5		
6. MICROBIOLOGICAL RES AUTHORITY				4	3	7		
7. ANTHONY NOLAN BONE MARROW TRUST			14					
8. ROSLIN INST EDINBURGH		10						
9. SCOTTISH CROP RESEARCH INST		9						
10. MEAT AND LIVESTOCK COMMISSION			4					
11. THROMBOSIS RES INST		4						
12. TAYSIDE UNIVERSITY HOSPITALS				4				
13. HORTICULTURE RES INTERNAT		3						
14. MATHILDA &TERENCE KENNEDY INS		3						
15. ST JAMES AND SEACROFT UNIVERSITY TRUST			3					
16. YORKSHIRE CANCER RES				4				

Chapter 8: What is the role of industry? How much cross-sector collaboration takes place?

Patent applications provide information regarding the inventor and the applicant for the patent. The inventor is the person or persons who carried out the work described in the patent application. This is usually the research scientist working for a company or for a university or other research institute. The applicant is the entity (usually a company, university or research institute) who is applying for the patent and who will become the owner or proprietor of the granted patent. The inventor is often an employee of the applicant. The applicant can also be referred to as the assignee of the patent as they are the company or other entity to which ownership of the patent, once granted, will be assigned.

By considering the country of origin of the inventor and/or that of the proprietor/assignee of the patents applied for in each of the areas of relevance to Genomic Medicine one can get an insight into the amount of research and development that is taking place in a particular country.

Tables 8.1 to 8.8 below show the country of origin for the patent assignee and country of origin for the inventor expressed as a % of the total number of patent applications[19] for each of the eight areas of technology relevance to the filed of Genomic Medicine. The Tables have been ordered on the basis of the UK ranking for each area.

The inventor country data gives an indication of work that is carried out in the UK that leads to a patent application. The inventors named on the patent applications from the UK may be working for a UK or a non-UK based company.

Table 8.1 Top 10 applicant/inventor countries in the field of **SNP/haplotypes**

Patent Assignee Country	No. applications	% of total	Inventor Country	No. patent applications	% of total
United States	8160	51%	United States	8436	47%
Germany	1267	8%	**United Kingdom**	**1489**	**8%**
United Kingdom	**1167**	**7%**	Germany	1423	8%
Japan	781	5%	Japan	902	5%
France	716	4%	France	799	4%
Canada	455	3%	Canada	618	3%
China	439	3%	China	475	3%
Switzerland	417	3%	Netherlands	393	2%
Netherlands	330	2%	Australia	376	2%
Australia	263	2%	Switzerland	312	2%

[19] The data used to prepare **Tables 8.1 to 8.8** is taken from the country code field in the EPODOC database. However, this is not fully populated for all patent applications and these figures and % values are indicative only.

Table 8.2 Top 10 applicant/inventor countries in the field of **protein-protein interactions**

Patent Assignee Country	No. applications	% of total	Inventor Country	No. patent applications	% of total
United States	10939	58%	United States	11257	54%
Germany	1238	7%	Germany	1449	7%
United Kingdom	**1126**	**6%**	**United Kingdom**	**1425**	**7%**
Japan	1062	6%	Japan	1266	6%
Canada	663	4%	Canada	885	4%
France	534	3%	France	563	3%
Switzerland	409	2%	Switzerland	443	2%
Netherlands	341	2%	Australia	350	2%
Denmark	323	2%	Denmark	345	2%
China	231	1%	Netherlands	337	2%

Table 8.3 Top 10 applicant/inventor countries in the field of **modified animals**

Patent Assignee Country	No. applications	% of total	Inventor Countries	No. patent applications	% of total
United States	4746	56%	United States	4947	52%
Japan	838	10%	Japan	992	10%
United Kingdom	**588**	**7%**	**United Kingdom**	**739**	**8%**
Germany	408	5%	Germany	473	5%
France	373	4%	France	403	4%
Canada	326	4%	Canada	382	4%
Sweden	154	2%	Australia	217	2%
Australia	151	2%	Sweden	202	2%
Switzerland	129	2%	Netherlands	154	2%
Netherlands	116	1%	Switzerland	138	1%

Table 8.4 Top 10 applicant/inventor countries in the field of **genes and regulatory sequences**

Patent Assignee Country	No. applications	% of total	Inventor Country	No. patent applications	% of total
United States	8074	49%	United States	8259	46%
Japan	1472	9%	Japan	1672	9%
Germany	1343	8%	Germany	1492	8%
United Kingdom	**977**	**6%**	**United Kingdom**	**1101**	**6%**
France	806	5%	Canada	821	5%
Canada	617	4%	France	721	4%
China	470	3%	China	503	3%
Switzerland	409	2%	Korea	410	2%
Korea	335	2%	Netherlands	387	2%
Netherlands	293	2%	Switzerland	333	2%

Table 8.5 Top 10 applicant/inventor countries in the field of **protein structure**

Patent Assignee Country	No. patent applications	% of total	Inventor Country	No. patent applications	% of total
United States	2403	54%	United States	2474	49%
Japan	378	8%	Japan	439	9%
Germany	324	7%	**United Kingdom**	**435**	**9%**
United Kingdom	**312**	**7%**	Germany	351	7%
France	119	3%	Canada	155	3%
Canada	117	3%	France	153	3%
Netherlands	115	3%	Netherlands	132	3%
Switzerland	114	3%	Denmark	117	2%
Denmark	99	2%	Belgium	105	2%
Belgium	85	2%	Switzerland	95	2%

Table 8.6 Top 10 applicant/inventor countries in the field of **gene expression profiles**

Patent Assignee Country	No. applications	% of total	Inventor Country	No. patent applications	% of total
United States	14717	58%	United States	15896	56%
Japan	1841	7%	Japan	2220	8%
Germany	1713	7%	Germany	1999	7%
China	1206	5%	**United Kingdom**	**1366**	**5%**
United Kingdom	**1156**	**5%**	China	1266	4%
France	910	4%	Canada	902	3%
Canada	702	3%	France	854	3%
Netherlands	473	2%	Netherlands	522	2%
Korea	387	2%	Korea	477	2%
Switzerland	363	1%	Australia	440	2%

Table 8.7 Top 10 applicant/inventor countries in the field of **gene related algorithms/software**

Patent Assignee Country	No. patent applications	% of total	Inventor Country	No. patent applications	% of total
United States	5673	56%	United States	6407	54%
Japan	796	8%	Japan	917	8%
Germany	585	6%	Germany	640	5%
China	475	5%	**United Kingdom**	**534**	**5%**
United Kingdom	**423**	**4%**	China	510	4%
France	306	3%	Canada	372	3%
Canada	283	3%	France	348	3%
Switzerland	170	2%	Switzerland	213	2%
Netherlands	157	2%	Korea	184	2%
Korea	139	1%	Israel	161	1%

Table 8.8 Top 10 applicant/inventor countries in the field of **human genes**

Patent Assignee Country	No. patent applications	% of total	Inventor Country	No. patent applications	% of total
United States	8254	64%	United States	8478	60%
Japan	1053	8%	Japan	1247	9%
China	1009	8%	China	1044	7%
Germany	561	4%	Germany	682	5%
France	359	3%	**United Kingdom**	**431**	**3%**
United Kingdom	**316**	**2%**	Canada	350	2%
Canada	271	2%	France	345	2%
Switzerland	148	1%	Switzerland	169	1%
Australia	126	1%	Australia	168	1%
Sweden	122	1%	Sweden	159	1%

It is clear from the inventor country data from all eight tables that the UK is a good location for carrying out research in all the areas of technology of relevance to Genomic medicine. The UK is ranked in the top 5 for all eight areas of technology. The US is ranked first in all eight areas, though this is not surprising given the amount and number of US patent applicants in each area of technology (as discussed in Chapter 6). The UK is ranked 2nd in terms of inventor country for **SNP/haplotypes** and 3rd for **protein-protein interactions** and **modified animals** indicating particular strengths in these areas.

The patent assignee country data gives an insight into the importance that companies in that country place on a particular area of technology. Such companies are keen to have ownership of the technology described in the patent if they consider such technology to be important for their future commercial operations. Companies can achieve ownership of such technology through funding work to be carried out in collaboration with scientists in the academic sector (universities, public research institutes) or by carrying out the work themselves in their own research facilities. The analysis described in Chapter 7 has shown that UK companies use both approaches.

Tables 8.1 to **8.8** indicate that UK companies consider the areas of technology of relevance to Genomic Medicine to be important. UK patent assignees are ranked in the top 6 in each area of technology and these rankings closely follow those for the inventor country data discussed above. The patent assignee country ranking is generally the same or one place lower than the inventor country ranking for the same area of technology. In the areas of **modified animals, protein-protein interactions** and **genes and regulatory sequences** both are equally ranked (see **Tables 8.2, 8.3** and **8.4**), whereas as in the other five areas studied the patent assignee country ranking was one place lower than the corresponding inventor country ranking, e.g., the UK ranks 2nd as inventor country and 3rd as for **SNP/haplotypes** patents (see **Tables 8.1** and **8.5 to 8.8**). This indicates a good correlation between where the work described in the patent has been carried out and the importance attached to its ownership.

The data also shows that China is emerging as a research centre in these areas of technology (as measured by the data on inventors) and also that Chinese companies are playing a leading role in carrying out and commissioning or funding research in these areas (as measured by the patent assignee data).

As was noted in Chapter 6, all the main pharmaceutical companies from other European countries are also involved in work in these eights areas of technology. This is confirmed by both the inventor country and patent assignee country data in **Tables 8.1** to **8.8** where France, Germany and Switzerland are all ranked within the top 10.

In all the areas of technology considered, the UK or Germany is the top ranked European country.

Chapter 9: What are the current research priorities?

In order to get an insight into what are the current research priorities in the eights areas of technology of interest to Genomic Medicine, it is possible to analyse published patent data in terms of how the invention it describes is classified to determine what are the key elements of the invention claimed and where the applicants interest appears to lie.

All eight areas of technology were analysed and the ten most frequently used classification terms were identified for patents filed in these areas over the last 10 years. These classification terms[20] which are explained in words on each of the Figures 9.1 to 9.8 provide a greater insight into the specific subject area of the invention. It should be noted that the same patent application may be classified using more than one classification mark in order to identify all the elements of an invention. For example, a patent for a diagnostic method of detecting gene expression may also include the computer-based data analysis methods to interpret the results. In addition, keywords as well as classification terms were used to select the patents in each of the 8 main subject areas. This means that where a classification term appears in more than one subject area, the number of patents will not necessarily be the same in each graph. For example, probes for detecting cancer may be directed towards detection of SNPs, detection of changes in gene expression or both.

Although I include the figures for 2005 and 2006, as noted earlier, these figures may not be complete. Thus Figures 8.1 to 8.8 can be used to indicate the relative trends between subjects, rather than the absolute patent filing trend.

[20] Classification terms, referred to as ECLA classification marks, use a hierarchy of combined letter and numeric codes to identify a particular feature of an invention. ECLA classification terms are applied to every patent application to identify all the elements of interest in the invention including its application/use. There is often a delay between publication and assignment of all the classification terms to a patent application. Hence the figures for 2006 are not likely to be complete.

1. Human Gene Patents

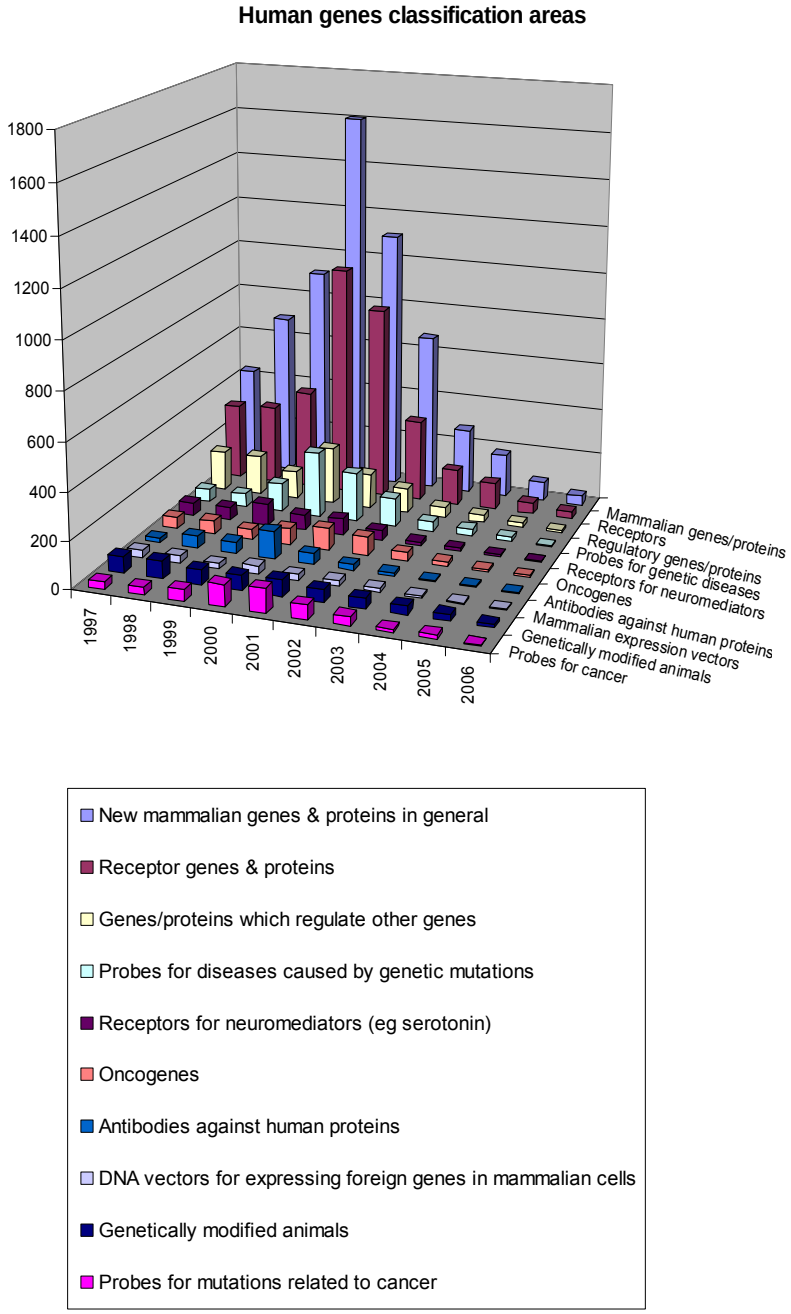

Figure 9.1 Classification of patents for **human genes**

The number of patents for new mammalian genes and proteins peaked in 2000, with a rapid decline since. This is likely to reflect the declining number of new human genes still to be identified following the Human Genome Project. In addition, this group of patents includes patents for genes of unknown function, or patents claiming large numbers of genes – developments in patent office practice in many countries have meant that patent applications of this type are unlikely to be granted. Patents relating to

specific types of human gene generally show a similar pattern, although the relative decline is generally less steep. Cell surface receptor proteins are the molecules which receive signals transmitted by hormones and are of particular interest as drug targets. One class of such receptors of particular pharmacological interest is the receptors for neuromediators – these are the targets of drugs such as Prozac (RTM) and Seroxat (RTM).

2. Genes and Regulatory Sequences Patents

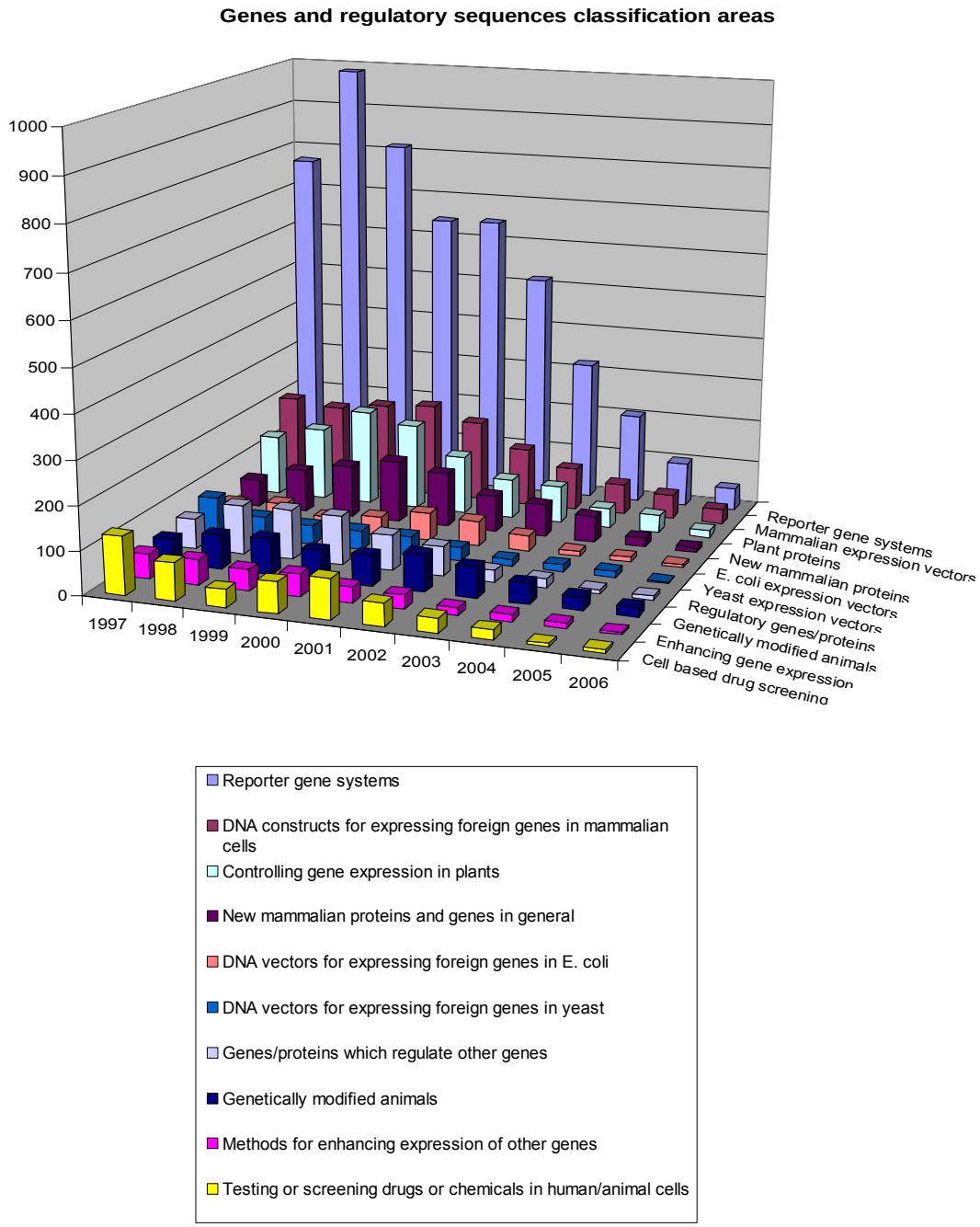

Figure 9.2 Classification of patents for **genes and regulatory sequences**

Patents in this group relate to the use of recombinant DNA technology to express genes and produce proteins in different organisms and cells (for example for producing medically important proteins in a foreign host cell). It also includes analysis of the regulatory sequences of genes. This is of great importance in understanding the molecular basis of cell biology, development and disease, and in developing novel therapies. In addition, identification of regulatory DNA sequences allows more efficient production of recombinant proteins. For this reason, this area of technology includes some patent applications relating to gene expression in organisms such as bacteria, yeast and plants, which may be used for the production of medically important proteins. The largest class of patents concern reporter gene systems, which use easily detectable genes for measuring whether a DNA sequence affects gene expression, typically in *in vitro* cell culture assays. Patents in this area have been in steady decline from 1998, which may indicate that this is a relatively mature technology – there are several widely used and effective reporter gene systems. Patent applications relating to in vivo gene expression systems in transgenic animals show a later peak of around 2002/2003, and a less steep decline, reflecting the continuous development of this technology.

3. SNP/Haplotypes Patents

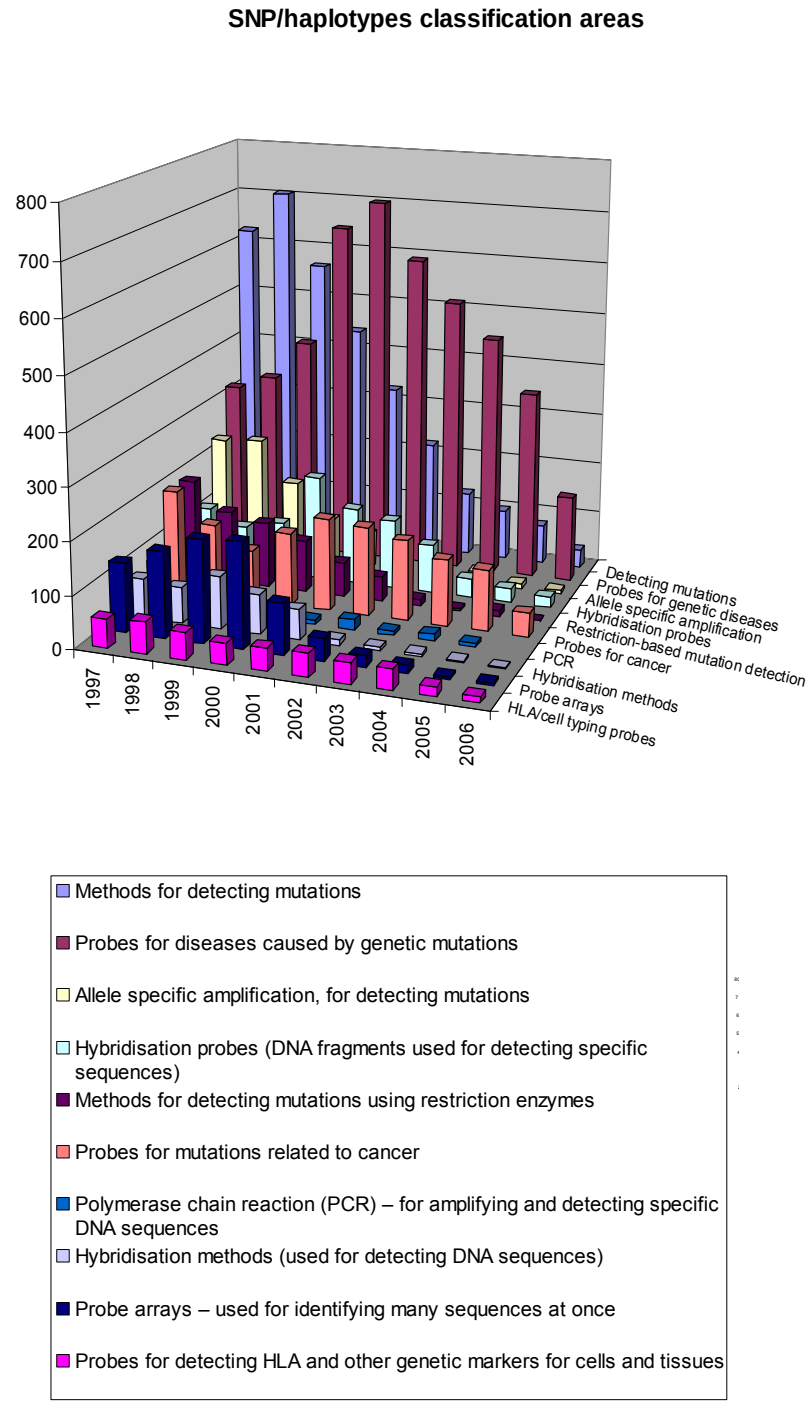

Figure 9.3 Classification of patents for **SNP/haplotypes**

Single nucleotide polymorphisms (SNPs) are simply single differences or mutations in a given gene sequence within the human populations – millions have been identified and a great deal of work has gone into identifying them, improving the methods for SNP detection and investigating associations between SNPs and human diseases. Very often diseases are associated with particular patterns of linked SNPs – these groups of mutations are known as

haplotypes, and detection of these is technically more complex. Within this area, it is clear that the numbers of patents for mere detection of SNPs has been in steady decline since 1998. This may in part reflect actual research trends and also patent office practice – patent applications which simply identify large numbers of SNPs are unlikely to be granted. The focus of activity appears to have switched towards diagnostic methods based on discoveries of correlations of SNPs and haplotypes with diseases, and in particular cancer – these now represent the majority of patent filings in this area. Cancer diagnostics in particular have shown very little decline in patent filings since 2001 (unlike the majority of biotech fields), reflecting the clinical need for cheap and reliable early screening tests for cancer, given the importance of early diagnosis in successful treatment.

A very large number of mutations can be screened at once using microarrays – chips carrying hundreds or thousands of probes for different SNPs. Patent filings in this area peaked in 2000 and have declined rapidly since, which may indicate that this is now a mature technology. DNA-based cell and tissue typing – particularly using probes for human leukocyte antigen (HLA) genes – remains a very active area of research. This in part reflects the importance of immunological differences in HLA variations, which are very significant for graft rejection and responses to treatments (personalised medicine).

A more detailed look at the top 50 companies filing in the area of **SNP/ haplotypes** patents is shown in **Table 9.1**.

Table 9.1: The 10 most common specific areas of interest for patent applications filed by worldwide entities (companies, universities, public research institutes) in the **SNP/haplotypes** area of technology**.**

	Detecting mutations	Probes for genetic diseases	Allele specific amplification	Hybridisation probes	Restriction-based mutation detection	Probes for cancer	PCR	Hybridisation methods	Probe arrays	HLA/cell typing probes
GENAISSANCE PHARMACEUTICALS	8	223		121		15				14
EPIGENOMICS AG	73	25	4	2		23	1		34	
US GOVERNMENT	63	69	54	62	33	31	12		2	3
UNIV CALIFORNIA	99	50	16	16	12	80	7	4	4	2
ROCHE	73	43	102	36		8	80	11	4	46
AFFYMETRIX INC	126	16	5	14	6	3		7	100	3
UNIV JOHNS HOPKINS	114	24	20	7	50	115	14			
DU PONT	30		76	14	40		11	9		
ASTRAZENECA	**21**	**87**	**39**	**42**	**1**	**16**	**29**	**8**	**3**	
APPLERA CORP	21	54	7			2		11		
SEQUENOM INC	99	87	71	1	1	53		18		
GLAXOSMITHKLINE	**11**	**26**	**7**	**2**		**4**				
PFIZER	6	21								
ICI PLC	**63**	**52**	**53**	**78**	**37**	**5**	**47**	**20**		
MERCK & CO INC		12		2						
INST NAT SANT ET DE LA RECH ME	35	74	23	22	8			7	3	
SANOFI-AVENTIS		56	1	3						2
KEYGENE NV	14		28	1	50		22		15	
GENSET SA	47	27		11		17			11	
UNIV IOWA	9	10		61	25			1		2
CHIRON CORP	14		67		14	6		8		5
UNIV UTAH	36	29	12	9	9	25				1
PROMEGA CORP	34		35	21	2	15		21		
UNIV BRITISH COLUMBIA	8	40	13		7	4		1		3
GEN HOSPITAL CORP	24	37	18	4	14	9			1	1
PASTEUR INSTITUT	35	13	12	6	8			5		
DEKALB PFIZER GENETICS	2									
NOVARTIS AG	6	36				10				
MAX PLANCK GESSELLSCHAFT	20	11	19	12	10	5	4	9		
CORNELL RES FOUNDATION INC	27	12	7	2	10		10	7	25	
HARVARD COLLEGE	7	48	43	43	8		49			
WHITEHEAD BIOMEDICAL INST	32	29	5	18	1	18			5	1
WISCONSIN ALUMNI RES FOUND	30	4		6	11	1	10			
UNIV TEXAS	27	30	10	22	1	18	13	3		
UNIV STANFORD	16	3	9		6	2		6	2	1
HOPE CITY	16	11	23	9	2	11	4	3	4	3
BAYER AG		28	4	1		3			1	
SAMSUNG ELECTRONICS	5	15				14				
BAYLOR COLLEGE MEDICINE	9	25	37	20	6	8	8			
HITACHI	6			2	8	1		5		
ISIS INNOVATION	**9**	**36**	**5**	**11**		**2**	**3**		**6**	**1**
EPIDAUROS BIOTECHNOLOGIE AG		38		1		7				
VISIBLE GENETICS INC	27		50			23				26
EXACT LAB INC	48		18		4	9	2	4		
UNIV MCGILL	7	39	3			8				
CETUS CORP	26	13	32	6	25	3	42	16		33
UNIV YALE	28	4		8	8			19		2
CENTRE NAT RECH SCIENT	18	13	1	5		2			3	6
MASSACHUSETTS INST TECHNOLOGY	26	9	17	1	16	24		2		
NANOSPHERE INC	1							31	22	

4. Gene Expression Profiles Patents

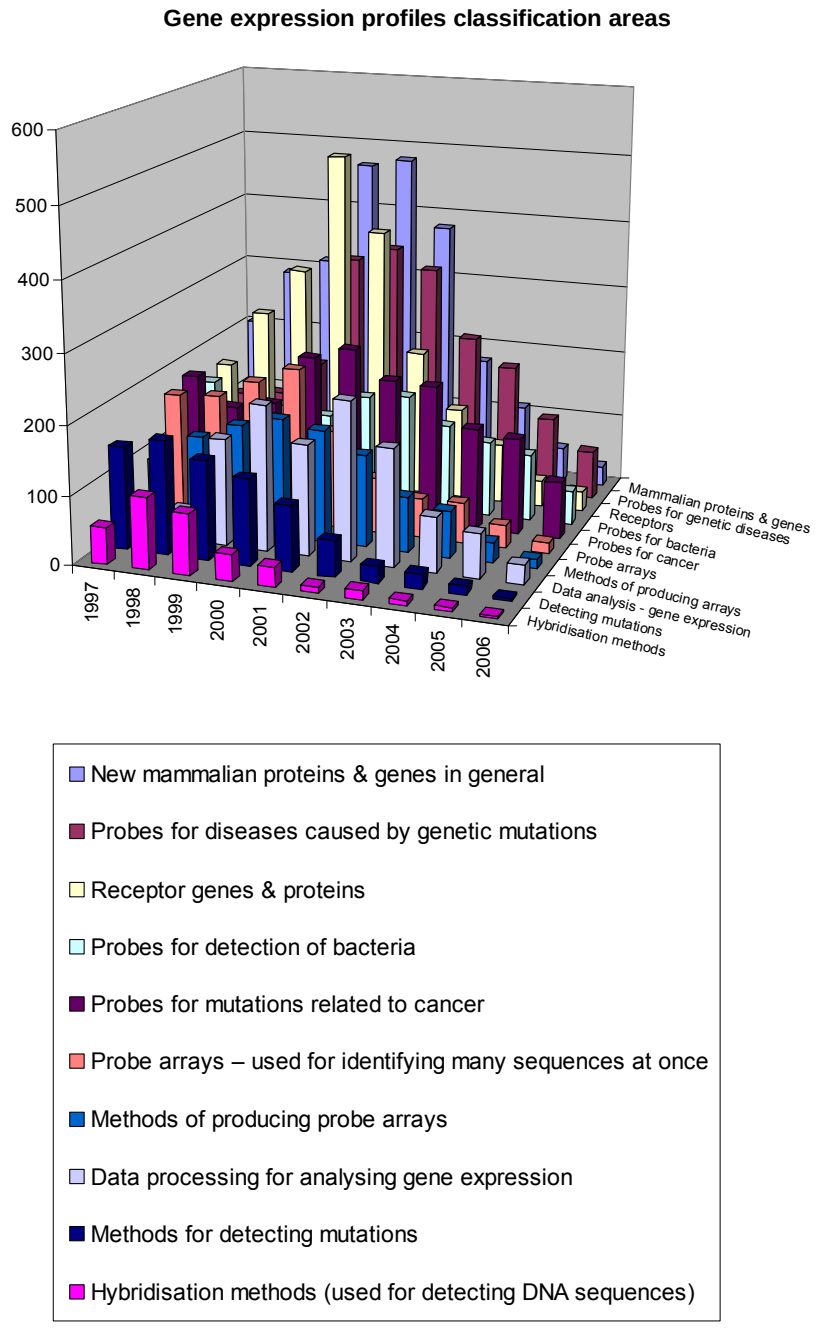

Figure 9.4 Classification of patents for **gene expression** profiles

This area has considerable overlap with the analysis of SNPs and haplotypes, particularly in terms of types of technology used to investigate gene expression. However, instead of looking at mutations at the DNA level, gene expression analysis measures quantitative differences in gene expression (resulting in changes in RNA or protein quantities). Patterns of gene expression are often correlated with specific diseases, while identification of

bacterial gene expression can be used for diagnosis of infectious diseases. Expression levels of particular genes and proteins may be diagnostic for specific cancers (for example, PSA for prostate cancer and CA-25 for ovarian cancer) and this is now the most significant single category in this field, with more filings than for diagnostic gene expression tests for all other diseases. Bioinformatics analysis of expression data is also a very active field.

5. Protein Structures Patents

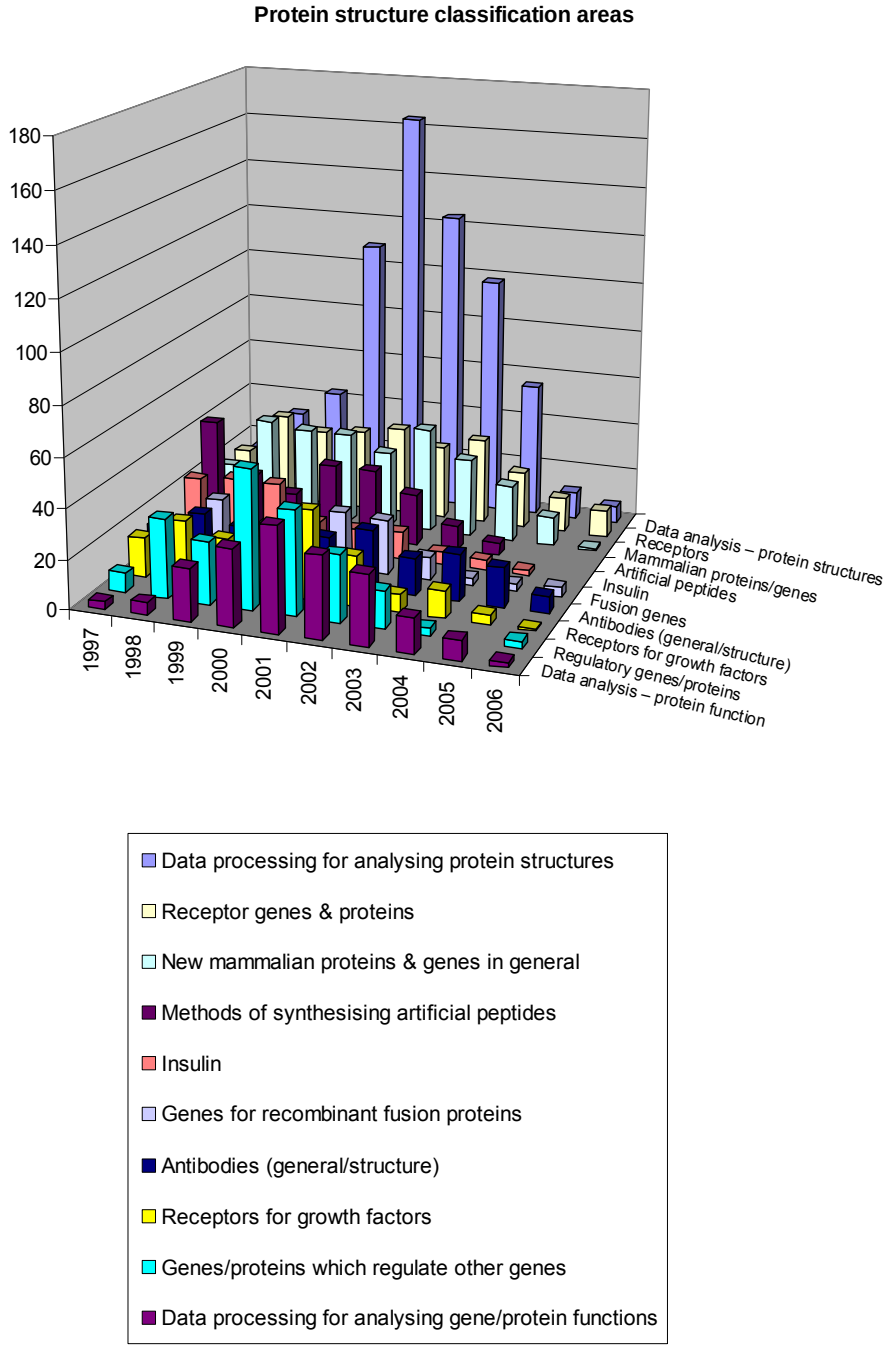

Figure 9.5 Classification of patents for **protein structures**

Analysis of protein structure facilitates the design of new drugs and the screening of old drugs for new purposes. This is particularly significant for cell surface receptors, which receive and transmit signals between cells and are very important as drug targets – patent filings in this area have remained strong. Structural analysis of antibodies also remains a very active field – this is important for new biological drugs. Patent applications for computer based protein structure and function analysis, on the other hand, rose rapidly to a peak in 2001 but have since declined. This may in part reflect the difficulties of getting bioinformatics patents in Europe.

6. *Protein-Protein Interactions patents*

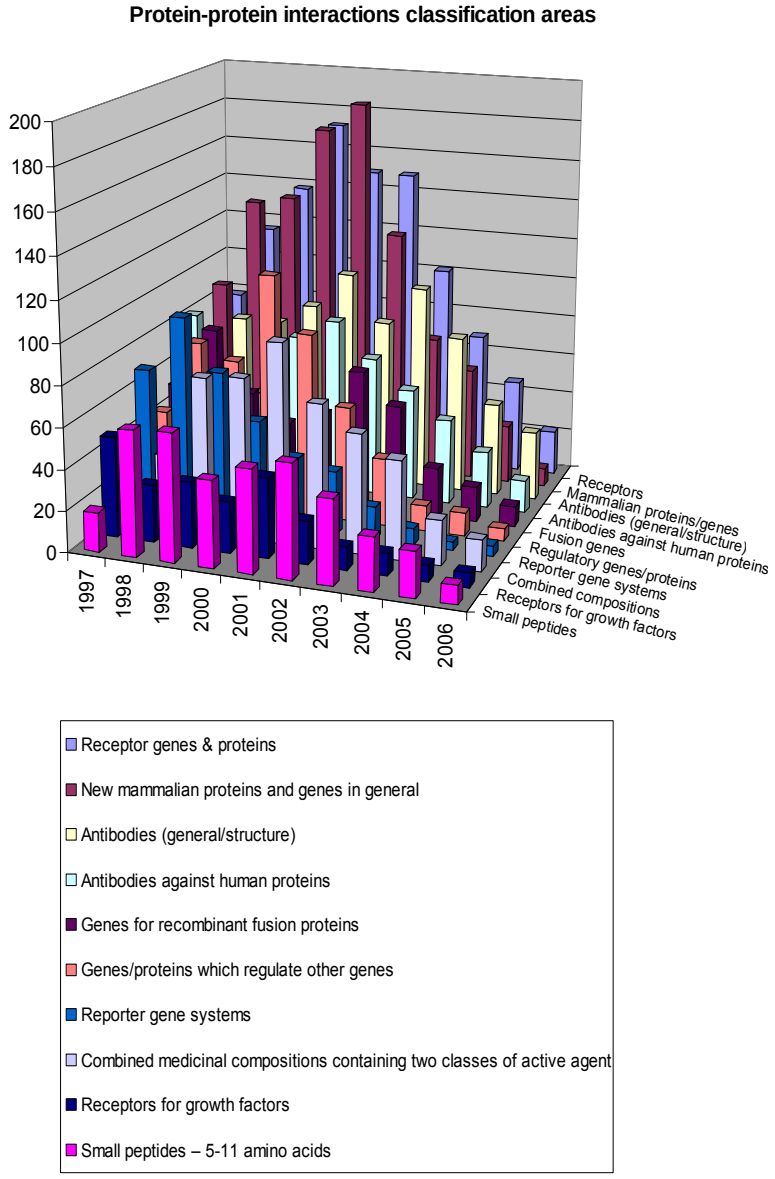

Figure 9.6 Classification of patents for **protein-protein interactions**

Following the sequencing of the human genome, there has been a switch in focus from how genes interact (genomics) and the investigation of individual proteins to the study of the interaction of proteins ("proteomics") – patent filings in this area have remained strong, and generally show a later and broader peak than other biotech fields. Patents relating to the study of protein interactions in general peaked in 2001 and have declined since, but patent filings relating to interactions of specific groups of proteins (for example, receptors and their signalling pathways, or antibodies and their target antigens) remain strong.

7. Modified Animals Patents

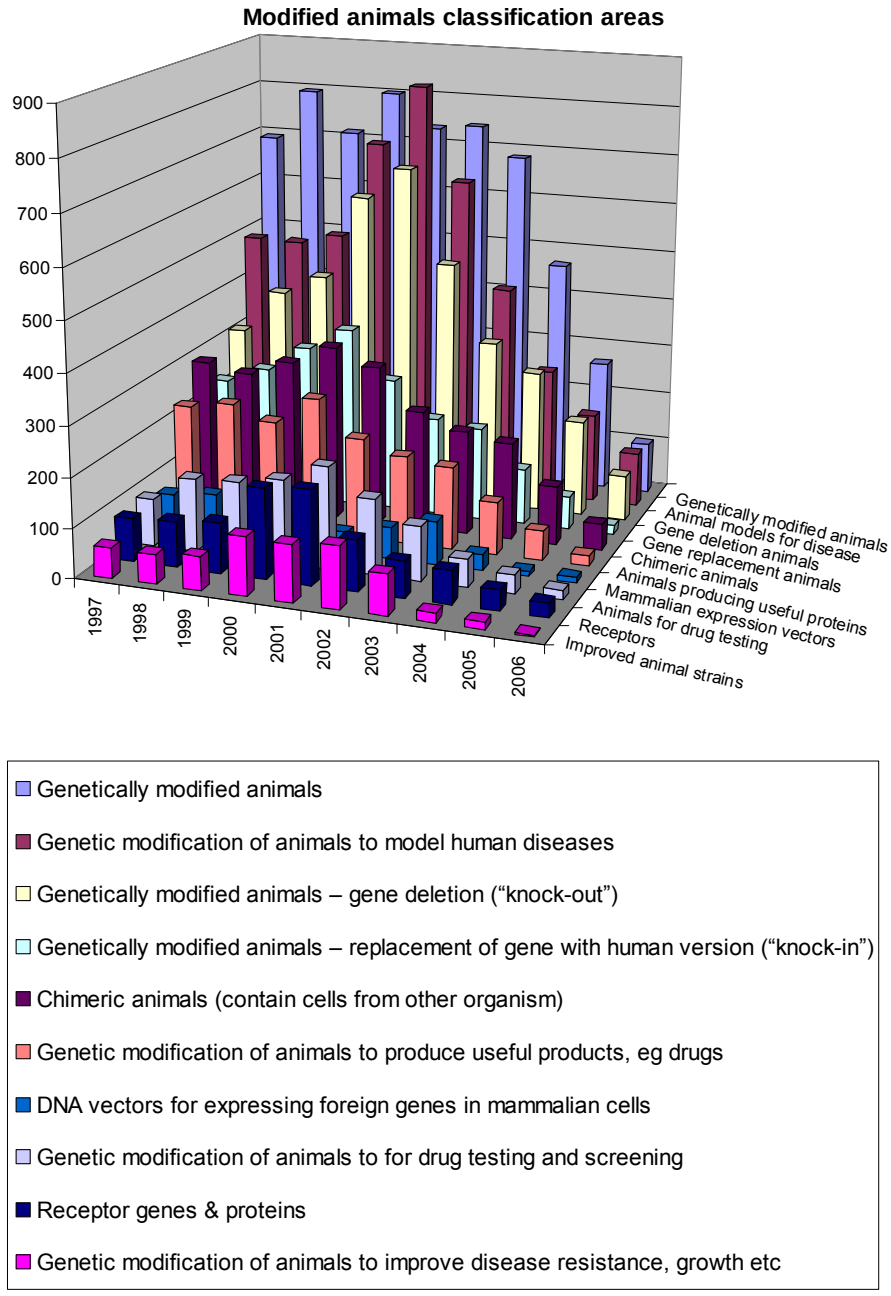

Figure 9.7 Classification of patents for **modified animals**

Patent applications relating to modified animals (primarily transgenic mice) show a broad plateau of activity from 1999-2003 and this is still a very active field. There appear to be few significant differences in the trends shown for the different branches of this technology, which include transgenic animals designed to model human diseases, "knock-out" animals which are engineered to lack a specific gene, "knock-in" animals where the native gene is replaced with the human equivalent, and chimeric animals containing cells from another animal species.

8. Gene related algorithms/software Patents

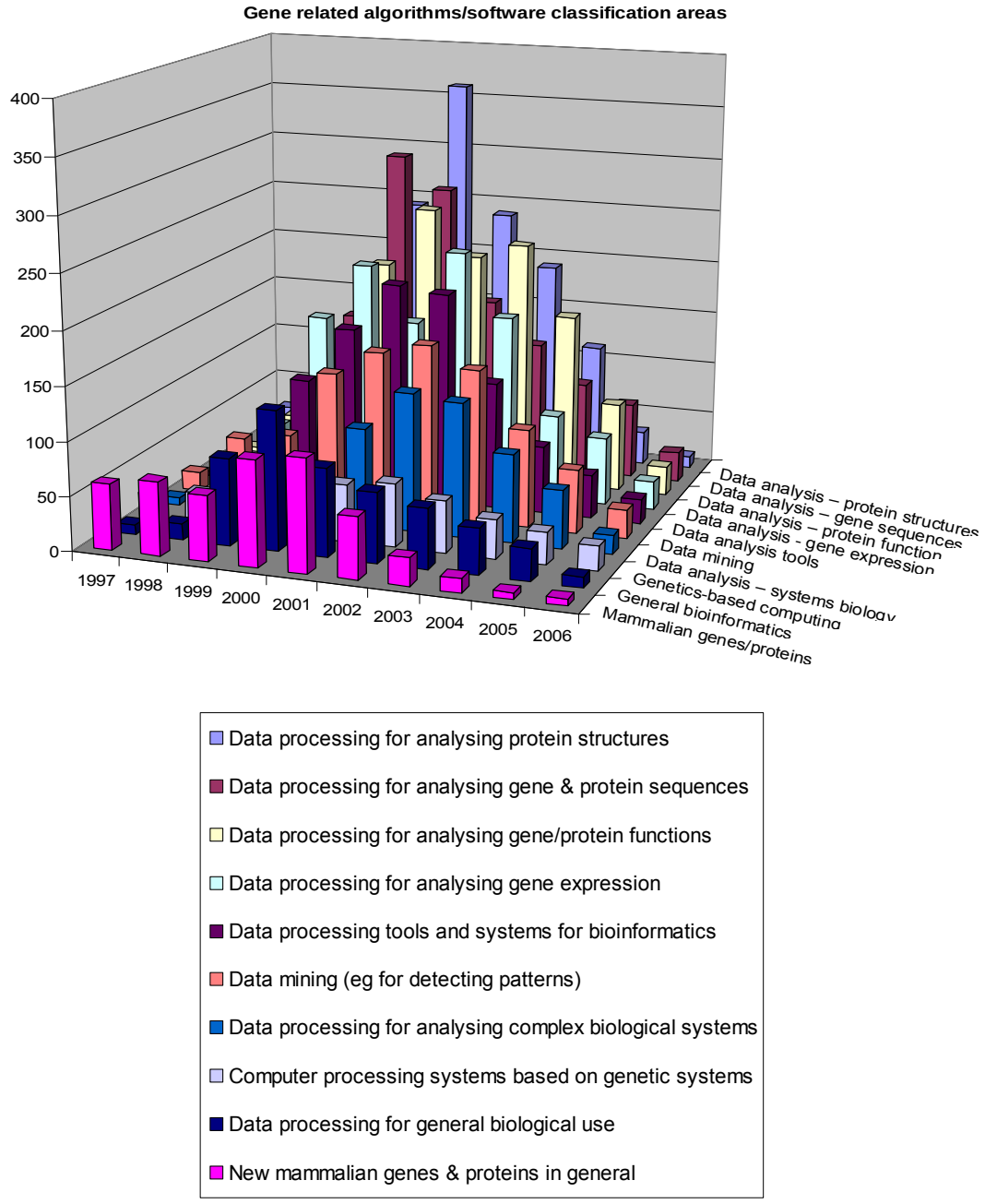

Figure 9.8 Classification of patents for **gene related algorithms/software**

Bioinformatics patenting was relatively insignificant 10 years ago, but increased very rapidly to peak around 2001, since when it has declined quite rapidly. This may in part reflect the difficulties of getting bioinformatics patents granted, particularly in Europe (including the UK), where inventions which solely relate to mathematical models or computer programmes are not patentable. Most of the subgroups within this field follow this broad trend, though the peak of activity for gene sequence analysis was slightly earlier (reflecting the trend for gene and protein discoveries). The use of bioinformatics to investigate the function of proteins, on the other hand, has a later peak and remains a very active field, as does the analysis of complex biological systems. Computer-based technology clearly plays a very important role in biomedical research, but at the same time genetic knowledge is also informing software development through the development of computer systems based on biological models – activity in this field has been very significant in recent years.

Chapter 10: What opportunities are there for diagnostics, therapeutics and prognostics – now and in the future?

Cancer Diagnostics

While it is not possible to answer the above question directly from analysing the Genomic Medicine patent landscape, it is possible to look at specific areas of interest within an area of technology of relevance to Genomic Medicine to see if and where patents which relate to diagnostic and prognostic probes for specific diseases are classified.

One disease where there is a particular interest in the development of diagnostics is cancer. There are two areas of technology where inventions which describe probes for cancer are classified. **Table 10.1** (see Annex to Chapter 10) lists all the companies, universities or research institutes/charities that have filed patents in the areas of **SNP/haplotypes** and **Gene expression profiles**, specifically directed towards cancer, its diagnosis and/or its prognosis. Taken together these two areas of technology provide ways to utilise developments in genomic analysis technology to identify predisposition to cancer, to detect and identify cancerous cells in the body, and also to indicate the stage, prognosis and optimum therapeutic strategy for cancer. Cancer diagnostics have been chosen as a case study as this is a specific area in which patenting activity has been highly active and remains so, despite the recent down-turn in patent applications in some other fields of biotechnology.

Moreover, cancer diagnostics is an area in which Genomic Medicine has already been at the heart of significant developments which have already impacted on treatments and survival rates, and more developments are in the pipeline. For example, predisposition to breast cancer caused by mutations in the *Brca-1* and *Brca-2* genes can be determined and more intensive screening, or even prophylactic surgery, can be instigated. Survival rates for most cancers are critically dependent on the stage of the cancer at diagnosis and aberrant expression of genes and proteins (e.g. CA-125 for ovarian cancer) can be an invaluable diagnostic indicator. The development of cancer is in most cases caused by multiple genetic changes, and can cause changes in expression in multiple genes, and so microarray technology may have an important diagnostic role to play.

Moreover, molecular characterisation of the cancer is important for determining the optimum therapeutic approach – for example, Herceptin (RTM) is only effective for the treatment of breast cancer where the cancer cells over-express the ErbB2 receptor protein. In addition, one of the major challenges in prostate cancer treatment is distinguishing between slow growing cancers (for which no treatment may be needed or desirable for

elderly patients) and more aggressive cancers that should be targeted by surgery, radiotherapy or hormone treatment.

Of the 313 entities worldwide that have applied for patents concerning cancer diagnosis or prognosis and are listed in **Table 10.1**, a total of 19 are UK-based. **Table 10.2** below shows all the UK entities (companies, universities or research institutes/charities) that have filed patents concerning cancer diagnosis or prognosis These UK based entities represent a mixture of small biotechnology companies, large pharmaceutical companies, universities, cancer charities and public research institutes.

Table 10.2: Numbers of Patent Applications filed by UK entities for **Nucleic acid-based Cancer Diagnostics.**

	UK COMPANY/UNIVERSITY/ INSTITUTION NAME	Probes for cancer[#]	Probes for mutations related to cancer[$]
1.	VISIBLE GENETICS INC	23	13
2.	ASTRAZENECA AB	16	4
3.	CANCER RESEARCH UK	15	2
4.	GLAXOSMITHKLINE	4	5
5.	GENOSTIC PHARMA LTD	7	
6.	ICI PLC	5	
7.	ISIS INNOVATION	2	3
8.	SYNGENTA AG	3	
9.	TAYSIDE UNIVERSITY HOSPITALS		3
10.	GEMINI RESEARCH LIMITED	2	
11.	RANDOX LAB LTD		2
12.	UNIV LONDON	1	1
13.	UNIV MANCHESTER	2	
14.	UNIV WALES		2
15.	GEMINI GENOMICS PLC	1	
16.	UNIV BELFAST		1
17.	UNIV BRISTOL		1
18.	UNIV LEEDS		1
19.	YORKSHIRE CANCER RES		1

[#] Taken from the **SNP/Haplotypes** area of technology
[$] Taken from the **Gene Expression profiles** area of technology