



# Current and Future Developments in Genomics

## ► Summary

The publishing of the human genome sequence at the start of the millennium was an early landmark in the development of the science of genomics. Genomic science is, however, very much more than a single genome sequence, or even the many sequences that are now available. As an approach to biological and medical research and translation of the outcomes to the clinic, to industry and to other applications, genomics has underpinned and driven great changes. The scientific world cannot be the same again, and neither can society as the impact of genomics spreads from the laboratory to everyday life.

In the UK the Research Councils have made a major contribution to the advance of genomics through focused funding initiatives as well as the conventional funding mechanisms. The impact of this has been felt not only in the UK but also internationally, with UK researchers undertaking world-class research in areas such as functional genomics, bioinformatics, metabolomics and genomics-driven drug target discovery.

In the next ten years, genomic science will have an increasing impact beyond the laboratory and computer programme. It is likely that the technologies and methods of genomic science will be commonplace in hospitals and test laboratories, that they will contribute greatly to improved food and fuel supplies and, vitally, to our understanding of the impact of climate change and how to respond to it. The impact of the internationalisation of disease is likely to be addressed and reduced using genomic science, to the benefit of all of humankind.

To benefit from such potential advances, it is necessary for genomic science to continue to develop and mature. This requires continued funding commitment from bodies such as the Research Councils, supporting high class research in the UK.

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# 1

## ► Introduction

The science of genomics has emerged since the middle of the 1990s as the capability to obtain, annotate and interpret the sequence of the genome of entire organisms has developed. The early focus was on the sequence of the human genome, the initial draft of which was published in 2000, but the genome sequences of many different organisms have also been determined and made available. This gathering of genome-wide information led to the study of organisms from a whole genome perspective: a new science was born.

In recognition of the opportunities offered by genomic science, the research area in the UK has received significant additional funding since 1998 through the Comprehensive Spending Reviews. The money allocated to the Research Councils (BBSRC, EPSRC, ESRC, MRC and NERC<sup>1</sup>) for genomic and functional genomic science was distributed using their established funding mechanisms and has amounted to some £236m over four years<sup>2</sup>. Through these mechanisms, the UK research effort in the area of genomics, led by the Research Councils, has made a very significant contribution to the successes and developments in the field. Groups funded by the MRC, BBSRC and NERC have already made major advances in the sequencing of important genomes, with the ultimate aim of understanding gene function.

As a balance to the independence the Research Councils had in supporting genomic sciences, the Cross Council Genomics Coordination Committee (CCGCC) was established by the Research council CEOs in March 1999. The CCGCC had a number of aims intended to ensure that there was interaction and co-ordination within the UK publicly-funded research effort in genomics and the development of a future strategy for the science in the UK.

Several years after its establishment, the CCGCC considered the impact of the genomics funding and the direction in which it believed genomics was taking research and society as a whole<sup>3</sup>. This paper is an outcome of that consideration.

<sup>1</sup> BBSRC: Biotechnology and Biological Sciences Research Council, EPSRC: Engineering and Physical Sciences Research Council, ESRC: Economic and Social Sciences Research Council, MRC: Medical Research Council, NERC: Natural and Environmental Research Council.

<sup>2</sup> Specific funding allocations, in the order of £110 M, were made to these councils in SR2000 for genomic and functional genomic science. In SR2002 additional funds totalling £136 M were allocated to the MRC, BBSRC, NERC, ESRC and EPSRC and also the CCLRC for post-genomic and proteomic research

<sup>3</sup> The CCGCC organised two one day meetings in December 2005 and February 2006 to discuss the issues. The first was held with senior representatives of different research areas, with presentations from key scientists. The second was a discussion day, involving many of the attendees from the first meeting and additionally other stakeholders as well as UK representatives of non-Research Council supported areas.



# 2

## ► The achievements and impact of genomics so far

### 2.1 Sequencing and annotation

By the end of 2006, the genome sequence of many important and interesting organisms had been published, with still further genome sequences held in private and other organisms such as the gorilla due to have their genomic sequence released in the near future. For many other organisms there is some genome sequence available in the public domain. Various reasons have driven this expansion of published genomic sequence, not least the availability of substantial high throughput sequencing capacity at several centres around the world. There is also recognition that the availability of genome sequence information will bring benefit to humans and animals in terms of our understanding and treatment of both disease and health, and also in many other aspects of our lives.

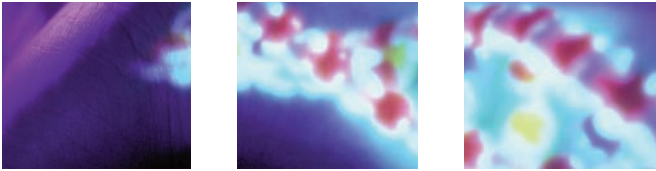
The UK makes a very substantial and significant contribution to the generation of sequence data and, perhaps even more importantly, its annotation. The Sanger Institute houses one of the premier sequencing centres in the world, responsible for sequencing a quarter of the human genome and part or all of the genome of many other organisms. The bioinformatics effort led at the European Bioinformatics Institute and Sanger Institute, both in Cambridge, is world class, and is supported by many other outstanding bioinformatics groups within the UK. Sequencing and annotation effort in the UK supported by the Research Councils has led to the publication of annotated genomes for a number of organisms that in turn supports many areas of biological and biomedical science in academia, industry and clinical practice.

### ► Genome sequences: a building block of genomics

Whilst the publication of the human genome sequence has been a primary focus of attention in genomics, it is the acquisition of genomic sequence data for many other organisms that has actually enabled genomics to develop. This is for a variety of reasons, including the greater ease of working with microorganisms, the importance of genetics in the emergence of new infectious agents and the need to use model organisms such as the mouse and rat in research to understand humans. In addition, for genomics to help us understand the place of humankind in the biological world, we need sequence from other organisms, both closely and distantly related to us.

The number of published genome sequences increases regularly, with new species and different strains or examples of already sequenced species being added all the time. MRC, BBSRC and NERC have funded all or part of the genome sequencing of important organisms such as humans (MRC), a bacterium that produces many natural antibiotics (BBSRC), the mouse (MRC), chicken (BBSRC), a plant that is used internationally as the model organism, and the tomato (BBSRC) and an important environmental alga (NERC).





## 2.2 The development of technologies

Arising from genomic knowledge have been the development and application of many techniques for measuring and analysing patterns of expression of other molecules at a whole genome or organism level, such as mRNA and proteins. Metabolomics too can be seen as a genomic methodology as it again takes advantage of the possibility of considering a whole organism and relating metabolic measurements to gene activity, function and expression. These capabilities are in place because of the timely development of various sophisticated technologies and techniques, such as mass spectrometry, laser-jet technology, vast improvements in imaging techniques, cheap computer power and storage and the movement of mathematics into biology. In all of these areas the UK has world-leading research groups and institutes, many benefiting from the extensive Research Council investment in genomics. These groups provide a knowledge and technology base essential to the research effort in the UK, and widely accessed both in the UK and internationally.

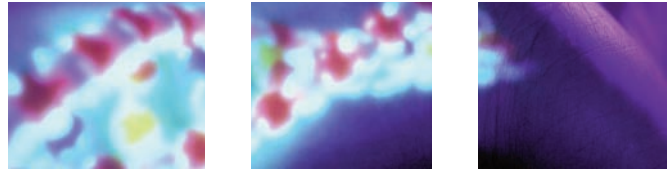
Accompanying the development of technologies has been the provision of important resources needed for genomic science. These include mutant and strain collections, extensive patient sample collections, microarrays, proteomics and genomic sciences facilities and structural biology. Many of these are supported by the Research Councils, and together they provide world-leading facilities.

### ► Bioinformatics

Bioinformatics is a vital tool, and area of research, for the development of genomic sciences. For the first time, biological research is able to generate quantities of data that rival, if not exceed, those of the physical sciences. Some of the tools already developed for addressing problems in particle physics, meteorology and astrophysics have been transferred from these areas and applied to genome sequence data and other genomic databases, but it is also necessary to develop a variety of new tools. Coupled with this is the entire problem of handling and archiving data sets and data bases on a scale that is unparalleled in the world. These databases are needed as the repository of developing information about different living organisms and represent vital common resources for all researchers to use.

The BBSRC, EPSRC, MRC and NERC have all contributed significantly, and continue to do so, to this vital area of activity. Examples of support include the NERC Environmental Bioinformatics Centre to support the work of the various NERC environmental genomics programmes, MRC funding to develop Fregene, software for simulation of sequence-like data for large genomic regions and large populations, required for the move into multiple resequencing projects, and BBSRC and EPSRC joint funding of the GeneWeaver project to develop a flexible system for automatic genome analysis and annotation.





### 2.3 “Functional genomics”

A principal early use of sequence data has been to greatly improve understanding of the information encoded in the genomes of organisms, and the function of that information, in particular the encoded proteins. This has often been referred to as functional genomics, and offers a way of identifying genes and proteins involved in particular events, or necessary for a specific phenotype. Current functional genomics research has provided knowledge and understanding of genes in pathogens and other micro-organisms, model organisms, plants and environmentally important species as well as humans.

Microorganisms in particular lend themselves to the investigation of issues at a whole genome level, such as studies identifying all genes involved in virulence for a given pathogen in a host organism. The value of model organisms such as the mouse is also amply demonstrated in developing tools for further research, such as the knock-out mouse libraries. These and model organisms such as the mouse, chicken and Arabadopsis, enable extensive study of many aspects of the biology of the organism, leading to a greater understanding of the issues such as disease, phenotypic traits and evolutionary development.

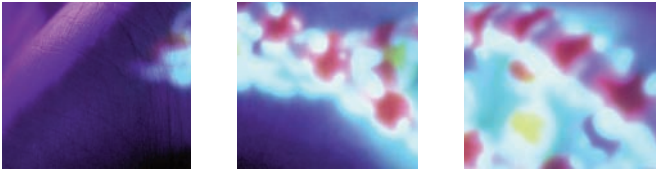
#### ► Genomic science: the role of model organisms

Model organisms are vital to research. They are used in scientific study on the basic assumption that the principles discovered through research on them will be applicable more widely, in particular to organisms of importance but that are difficult to study. There are model organisms in all fields of biological research and from all kingdoms. They act as models for humans, dangerous pathogens, difficult to cultivate plants and the unknown, amongst others. Model organisms make research easier, more cost effective and better.

Genomic science is no different. Sequence data, genomic tools, functional genomics and increasingly proteomics data have been gathered, developed and undertaken for model organisms in even greater profusion than for humankind. Research Council funding has made significant contributions in this area. For example, the MRC provided significant funding towards the sequencing of the genome of the primary mammalian model organism, the mouse. Further funding enabled a genome-wide gene knock-out programme in the mouse that led to the identification of 500 new mouse mutant strains for gene function studies, all made available to the scientific community. The Edinburgh Mouse Atlas has also been developed with MRC funding.



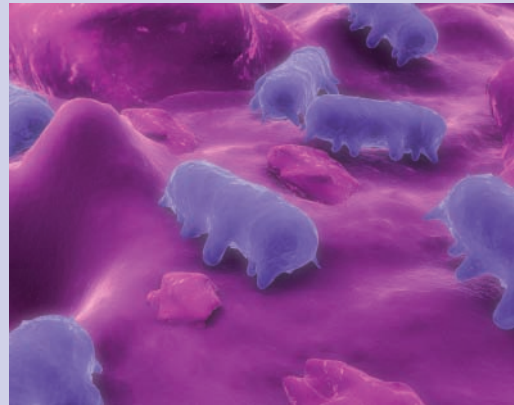
From such genomic and associated resources MRC-funded scientists have made significant discoveries of importance to humans, such as the first evidence that there may be a genetic cause for glue ear in children, made through work with a genetically modified mouse. Other genomic research using the mouse as a model for humans has explored the expression of genes during neural regeneration, a vital area of research for addressing spinal cord injuries. Further research with mice has demonstrated that some of the effects of prion infection can be reversed, suggesting this may be possible in humans infected with vCJD.



As the sequence of the human genome was being completed, and the early annotation was initiated, the assumption was that tens of thousands of genes would be found, many with unknown function. It was therefore something of a revelation to find that not only are there less than 30,000 genes in the human genome (at the end of 2006 there were just under 22,000 known genes) but that many of these genes could not possibly code for only a single protein. The importance of the 98.5% untranslated DNA thus emerged as a further aspect of genomic science. The control exerted over the process of gene expression in all its forms, epigenetics, is an area where the UK research effort is world-leading, with major advances being achieved in our understanding of small RNAs, gene imprinting and cell differentiation.

## ► Genomics and pathogens

Genomic sciences are particularly valuable when developing routes to preventing or curing infections. For example, a collaboration between the universities of Cambridge, Newcastle and Oxford, with Arrow Therapeutics, funded by the BBSRC and DTI, has used the genome sequence of *Salmonella* to identify novel vaccine targets against the pathogen in mice. The most promising of these are now being studied in farm animals in a project funded by BBSRC. In another project, again funded by BBSRC and DTI, a collaboration between Oxford University and Prolysis has identified targets in *Staphylococcus aureus* that are being used to develop new anti-MRSA treatments.



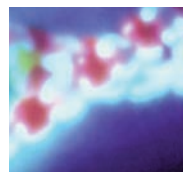
## 2.4 Application of genomic science

Developing understanding of gene function is leading to significant insights into human health and disease, crop plants and our understanding of environmental response to events such as the erosion of biodiversity and climate change.

### *Human disease and health*

Many diseases have a genetic component, not just the monogenic disorders such as cystic fibrosis and Huntington's Disease. Genomics has provided a mechanism for exploring the genetics of complex disorders which have a genetic component but are not solely determined by this. These include important diseases of Western society such as Alzheimer's, heart disease, diabetes, cancer and asthma. Research Council support has contributed to the understanding of many of these. Human behaviour also has a genetic component, and genomics have given insight into areas such as depression and childhood learning and behavioural issues:

Infectious diseases remain the leading killer of humankind worldwide, and genomics has offered vital opportunities for advances in understanding pathogens, host: pathogen interactions, epidemiology, and pathogen response to antimicrobial agents. The use of genomics is leading to the identification of novel targets for vaccines, antibacterial agents and antivirals. Research relating to a prospective 'flu pandemic and the emergence of new diseases such as SARS greatly benefits from the power of genomic technologies, and Research Council funding makes a significant contribution to these.



## ► SARS and HIV

With the outbreak of SARS in 2002-3 and the current concerns about avian influenza, the MRC and BBRSC are supporting a number of genomic science-based projects to advance our understanding of these and other new viral infections. Recent research funded by Research Councils, the Royal Society and the Wellcome Trust has shown how the mis-reading of the genetic code of viruses such as SARS and HIV enable modified proteins to be produced by the virus, helping the viruses to evade the immune systems of their hosts



### *Genomics and animals*

Understanding of animal health and disease similarly benefits from the science and technologies of genomics. Genomics is offering insights into desired traits in farm animals, the development of vaccines against important pathogens such as Salmonella and disease in dogs and other animals.

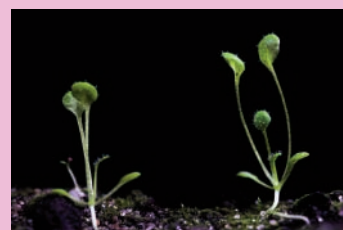
### *Understanding crops*

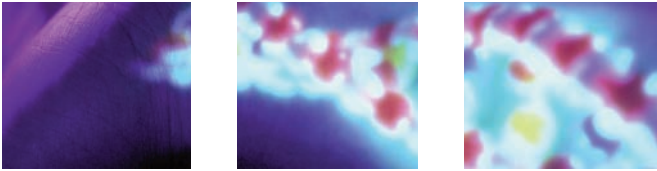
Plant genomics provides exciting opportunities to understand crop and other plants, and to improve these for the benefit of human and animal health and nutrition. Study of the genomics of the model organism Arabidopsis has led to insights into gene function in plants.

## ► Plants and genomic sciences

The world's population is growing inexorably and harvests worldwide are threatened by climate change. Global food security depends ultimately on growing enough crops. Economic, political and social factors are important, but sufficiency and sustainability of harvests are the primary needs. Genomic sciences offer a way in which we can identify and select crop traits and production systems that can increase yields in particular soils and climatic conditions, and reduce losses to pests and diseases.

Black rot is a bacterial disease caused by *Xanthomonas campestris* which can devastate and potentially destroy kale and cabbage crops in warm climates, such as East Africa. Control of this seed-borne disease is difficult as there is no effective chemical treatment. UK geneticists and pathologists are working with crop scientists in Kenya, using the latest genomic tools in brassicas and Arabidopsis, to identify genes that confer broad-spectrum resistance to black rot. This will enable more rapid breeding of resistance into local varieties, the large-ear variety, and to increase grain production in elite varieties.





### *Understanding the environment*

Genomics has exciting and important applications in our understanding of the environment, already making a contribution to our understanding of two major areas of environmental concern: the loss of biodiversity and climate change. For example, the definition of species is increasingly achieved at the genomic level, leading to increased understanding of biodiversity, evolution and the definition of species groups. Projects such as the joint NERC-BBSRC Ecological Dynamics and Genes (EDGE) programme derived from a genomics approach to identifying species in danger. Others explore interactions between different species, such as Research Council-funded genomic studies of an algal-infecting coccolithvirus that offers insights into the management of coastal algal blooms.

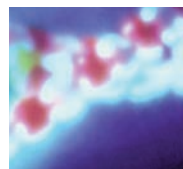
## ► Genomics, environmental health and pollution

Current approaches to addressing the consequences of pollution include determining the impact of specific toxic chemicals on ecosystem function. The Environmental Genomics programme lead by NERC has funded projects to assess the impact of chemical pollutants which engaged relevant industrial and regulatory stakeholders. One study addressed the specific effects of oestrogenic compounds in aquatic pollution which modify the sex of fish, which in turn has broad implications for conservation of wild species, as well as human health. Another study examined the biological impacts of terrestrial pollutants such as agrochemicals, cadmium and aromatic hydrocarbons. Using earthworms as a 'sentinel' species, environmental genomics researchers determined the biological significance and specific impacts of varying levels of pollution



### 2.5 Society keeps pace

The science of genomics presents new challenges to the way in which science and society interact, in the application of the science and in the understanding of what it is to be human. The development of understanding of the impact of genomics, necessary science governance systems and the public understanding of genomics is being addressed in the UK and elsewhere. The UK has an exemplary reputation in the development of ethical, social and legal implications of new biology, and is leading the way in many aspects of these in relation to genomics. Research Council funding has led to exploration of genomics and society in the UK and internationally, as applied to health, nutritional, industrial and policy issues amongst others.



## ► Genomics, environmental health and pollution

In the light of initiatives in biobanking (the collection, storage, processing and distribution of biological materials) in different social contexts, there have been calls for harmonisation between initiatives, both scientifically and ethically. ESRC-funded research has critically examined the meaning and potential of harmonisation and identified four different types of ethical impact in biobanking.

These are: varying academic and societal discussion in different countries; the development of new models of consent

and property in the genome; the possibilities of international ethical governance; and a shift in ethics from an individual-centred to a more community-centred approach. This shift informed the revision of the 1996 Human Genome Organisation Ethics Committee Statement on the Principled Conduct of Genetics Research. The research contributed to Professor Ruth Chadwick's winning of the World Technology Network Award for Ethics in 2005, and to an invitation to make a presentation to Unilever.



### 2.6 Conclusion

The skills, resources and technologies arising from the genomic science are being applied to virtually all aspects of biological investigation, to the benefit of humans, animals and the world around us. Research Council funding in the UK has made a significant difference in this country and internationally. This is an exciting time to be involved in such science



# 3

## ► Genomics in ten years time: the underpinning science

### 3.1 The importance of genome sequencing and annotation

Towards the end of the human sequencing project there was a view expressed that once the human genome sequence was available, supported by the genome sequences of the major model organisms and pathogens, then there would be little need for further sequencing capacity or effort. However it is being constantly demonstrated that there is great benefit in continuing the international genome sequencing effort. Significant genome sequences are being published on a regular basis, with the next milestone the release of the genome sequence for the gorilla. The key to the future is that the various techniques currently used within the field of genomic science will move forward as new and far more cost-effective technologies emerge. A vital example of this is the development of technologies for massive “resequencing” of genomes that will enable genome sequencing of many individual organisms. These guarantee that in 10 years time we will have an understanding of human variation at the genetic level within the species, and of how we are differentiated at the genomic level from other living things. Genomic sciences will not only influence our understanding of human variation, they will underpin a whole range of aspects of life and society.

### 3.2 The development of genomic technologies

Currently, many of the technologies and techniques used in support of genomic sciences are very expensive, available only to well-funded academic and industrial research groups. In addition, some of the technologies e.g. aspects of proteomics are relatively low throughput, nor are they adaptable to a high-throughput format which is not useful when addressing genome-wide questions. Other technologies, such as microarray techniques, are high throughput but generate quantities of data that require extensive bioinformatics and computer support.

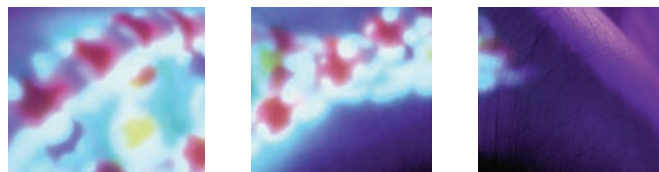
These issues limit the current use and application of genomic technologies.

The landscape has changed with respect to sequencing. With the 454 sequencing and other very high throughput-low-cost techniques much more can be done with the non-model species and metagenomics. There are bioinformatic challenges though; more sequences with lower read length (bigger jig-saw with smaller pieces). Therefore the technologies are more data rich. We need to ensure that we get knowledge so techniques for 'phenotypic anchoring' are required to assign functions to genes.

Also, with these high throughput techniques the days of the microarray might be numbered. There are sequence-based methods for assessing gene expression (SAGE etc.) that were limited due to the cost of sequencing. This is no longer an issue.

In the next ten years it is clear that many of the issues of cost and accessibility of genomic technologies will be resolved. In some areas the solutions are already in hand. Resequencing technology, the goal of the \$1000 human genome sequence, and increasingly cheap array systems, are already emerging. Familiarity with technology such as mass spectrometers and imaging makes these approaches accessible not only to research groups but to hospitals and routine testing laboratories. Different technologies are being explored to solve the problems of proteomic analysis, which will lead to cheaper, higher throughput systems. Miniaturisation, the ability to experiment with a single cell, the possibilities of using molecules as motors and machines will all provide sophisticated, targeted assay and experimental systems. A key area will be the availability of immense computer power and storage capacity at very low cost. The success of the computer industry in reducing costs and increasing capacity and speed, following Moore's law, has been vital in the development of genomics so far and will continue to be so.

A major developing issue is actually how to store, access and use the swathes of data emerging from ever more powerful genomic techniques. Currently this problem is effectively a debate, as the implications of, for



example, data quantities from “resequencing” emerge. However, during the next ten years a consensus will have to emerge, as the way in which data are used will be key to their usefulness to a wide range of non-specialists.

In ten years time many of the current genomic science research techniques and their descendants will be available for routine use. This will enable the translation of genomics research into far more common practice, in hospitals, doctors’ surgeries, environmental and food testing, animal welfare and other areas. Some techniques will have emerged that are so robust and cost-effective that they will be applicable in developing countries and in emergency situations, making genomic science truly global.

These developments in the technologies of genomic sciences are essential. Without them the benefits of genomic sciences will not be seen in the many ways described below.

### 3.3 Scientific progress

As befits a relatively new area of science, in ten years time genomics will cover more topics, and in greater depth, than at present. The basis of research into variation in genera, species, populations and individuals at the genetic level is already established, and will have progressed greatly. This will provide the foundation for many other areas of science.

Understanding of the function not only of genes but of all regions of the genome will have generated a significantly enhanced appreciation of the nature of DNA. Epigenetics has already been recognised as an important area of genomic science, but there is still a great deal to be understood about the role of all aspects of the genome, and how these are involved not only in the expression of a given phenotype, but in the development of the whole organism. Genomic science will contribute to our understanding of how whole organisms develop from the initial cell through all life stages. This work has started already with model organisms, but in ten years time will be based on a wider species base, offering the opportunity to understand at a much deeper level the function of genes, regulatory regions and the way in which external influences impact on them.

The genomic technologies available in the future ensure that it will be possible to establish methodologies to explore the association with a particular phenotype of every gene in a given genome. Thus it will be feasible to examine the association of all genes, and probably regulatory regions, with complex diseases such as Alzheimer’s and diabetes. Similar research will interrogate genes and regulatory regions for the links with desired and undesirable phenotypes, pointing the way to potential engineering of humans.

Research will also be in place to explore how genomic variation in populations influences response to a variety of treatments and insults. Whilst human genomic variation will be a driving force, in particular reflecting interest in response to different medical treatments, many species will be the subject of such study. The impact of changing climate and therefore environmental conditions on genomic population variation will also be an area of significant scientific advance, in particular as applied to issues such as biodiversity and crop development.

Such trait identification and manipulation is likely to be in place for commercially useful animals and crop plants, partly for human and animal benefit, but also for research relevant to humans. As a component of this, manipulation of the germ line DNA, an area of science related to genomics, is likely to be established in practical terms for mammals and humans. Determining the safety of such research may well be a significant area of investigation. This would be a component of a variety of long-term genomics research studies that would be in place, following funding of resources such as BioBank.



# 4

## ► 4. Genomics in ten years time: the impact

Given the anticipated advances in genomic science and technology, a variety of impacts can be anticipated. These will be relevant to virtually all aspects of human life and the world around us.

### 4.1 Human health and disease

#### *The personalisation of medicine*

The availability of genomic information, the understanding of the role of genes and DNA regions in disease and health will underpin a move to a far more personalised approach to diagnosis, treatment and prescription in managing human disease. Increasingly, pharmacogenetics – the identification of specific patient groups who will respond as a consequence of their genetic makeup in a particular way to a medicine or treatment – will drive clinical practice and the discovery and development of new medicines. Importantly, in ten years time genomic sciences will also have been applied to a number of crucial off-patent medicines, where benefits in terms of efficacy and safety can be identified. Such patient stratification will be driven by the scientific possibilities but also regulatory and economic pressures to ensure that medicines are efficacious and cost-effective, with reduced adverse reactions.

Clinical practice will also adapt to the greater personalisation of medicines. There will be more point-of-use testing, with clinical practitioners being guided not only by conventional biomarkers such as blood-pressure, but also taking into account genetic variation of the patient and the presence of novel biomarkers, many of which will have been identified through genomic science.

#### *The focus on health*

Whilst the presence of variant genes implicated in complex diseases such as diabetes and asthma does not guarantee that an individual will develop such conditions, many genes that point to potential health issues will have been identified and tests made available. Personalised genomic information will give individuals greater awareness of genetic predispositions they may have. Such knowledge, available from “pre-conception to grave” for those yet to be born today, will offer opportunities for lifestyle choices that may in turn influence the possible impact of deleterious gene variants, or unwanted traits. The benefits of understanding how genes and environment interact will be particularly seen in this area, as individuals are able to take more control of their own health and wellbeing.

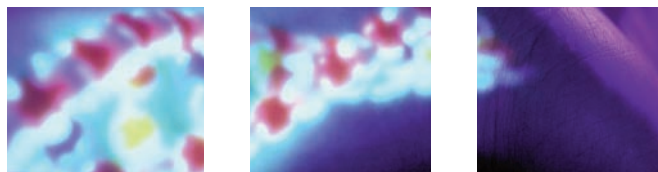
Individuals will be empowered by the level of information available to them on their health and wellbeing. This, coupled with the increasing complexity of medical sciences, will have an evolving impact on the relationship between clinical practitioners and their patients: there will be more of a partnership focused on a positive approach to managing an individual’s health thus preventing disease, as opposed to the classical doctor: patient relationship.

#### *The ageing population*

Increased health will lead to greater longevity for many people, which will only bring benefit if good health can be maintained throughout life. Genomic science will contribute not only to our understanding of how health is maintained in older age, but it will provide knowledge and understanding that will guide preventative, curative and palliative medicine in older people.

#### *Healthcare systems*

The changes in healthcare and management, accompanied by increased longevity of the population, are likely to offer serious challenges to the systems for the provision of healthcare in the UK in the future. Genomic science will provide insights into how best to manage and apply the resources of healthcare systems in order to maximise the health of the nation.



The changes driven by translation of genomics into clinical practice will also have significant impact on the training of doctors, nurses, pharmacists and other clinical scientists. Government policies relating to these, demographics and the general education of UK school and university students will increasingly need to respond to the impact of genomics-driven changes.

#### *Health and disease in the developing world*

Currently, the benefits of pharmacogenetics, genomic science and much modern biomedical research are primarily experienced in western nations such as the UK. In ten years time the benefits of genomic sciences will be experienced far more widely, and will be leading to significant improvements in the health of many societies. A further benefit will be a greater understanding of how new diseases emerge and spread, thus making the management of future pandemics, zoonoses and other as yet unknown pathogens more effective.

#### *The development of new medicines*

The process of discovering and developing new therapeutic molecules will change in response to many of the issues described above. The discovery of novel therapeutics will be highly dependent on genomic sciences, with increasing numbers of biological molecules being selected for clinical development as methodologies for their production and delivery are improved. Pharmaceutical companies will increasingly develop molecules that are targeted at subsets of a population who are identified through specific biomarkers. Safety and efficacy will be predicted from genetically-determined factors and regulators will expect such studies to be included in drug development.

## **4.2 Genomics and the economy**

#### *Sustaining and improving our food*

Genomic sciences will enable significant changes to crop plants for food, health and other economic areas such as fuels. Nutraceuticals – foods with health benefits – will be increasingly designed, often for use in conjunction with an awareness of an individual's genetic makeup. Crops making these, or with increased levels of these, will offer important advances in food quality as well as economic opportunities for the farming sector.

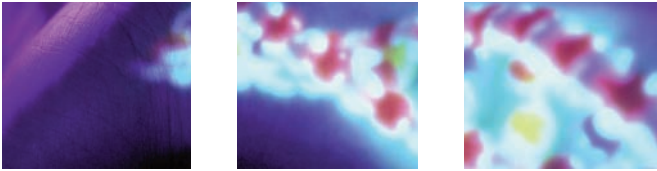
The pressures of climate change coupled with the understanding of plants derived from genomics will enable the development of crops that offer advantages in nutritional quality and agricultural efficiency. The current research to develop intelligent breeding approaches for animals as well as plants will enable increased efficiency of production of animals as well as crops, again with desired traits. Such research benefits will enable the UK to maintain appropriate levels of agricultural self-sufficiency whilst adapting to changing environmental circumstances.

#### *Animal health and wellbeing*

Whilst personalised healthcare for farm animals is unlikely, genomic science will have contributed to the development of novel treatments and, importantly, vaccines for farm animals. Vaccines will increasingly be used to improve animal health and to help reduce the risk of transmission of food-borne micro-organisms from the farm to humans.

Equally, genomic science will be increasingly used to develop understanding of companion animal health and wellbeing. Current research developing from the publishing of the dog genome will have led to the identification of gene associations for many canine diseases and of appropriate treatments. Similar research may well be progressing in areas of equine and feline health.

Animals are an important tool in various aspects of scientific research, including genomics. Whilst their use will still be necessary in ten years time, genomic and other sciences will have contributed to the development of some alternative techniques, and to a greater understanding of how to interpret data from simpler systems so that the numbers of animals included in research can be reduced.



#### *Non-food crops*

With the recognised pressure on energy sources, plants offer possible routes to alternatives over fossil fuel. Photosynthesis harnesses energy from the sun, and in ten years time increased understanding of these processes should be contributing to the development of novel fuels. So too should research to develop methods for converting plant biomass into fuels either directly or indirectly.

Plants also offer a novel route to production of biotherapeutic proteins and other valuable proteins that will be further enhanced in ten years time, and which UK agriculture will be positioned to exploit, bringing it economic benefit and strength.

#### *The industrial sector*

The translation of genomic sciences to the benefit of the UK will be driven by a mixture of the quality of the science, clinical and economic need and the strength of the relevant industrial sectors. These will be most able to take advantage of the developments of genomics if there are suitable structures for collaboration with academic research, and appropriate economic and regulatory frameworks that ensure that UK industry can compete with similar sectors internationally.

### **4.3 Social systems in the UK**

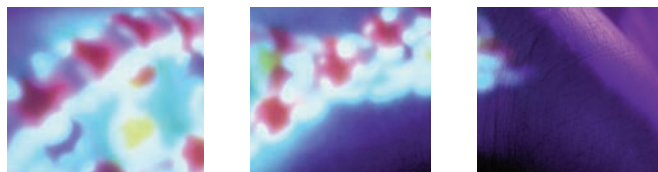
There is already a recognition that in the changing international economic climate the UK needs a very strong science base in order to ensure that economic and social development can be sustained. Genomic sciences will be one component of the increasing interaction between society and science that contributes to progress in the UK. However, in order to achieve this, there will need to be development of improved and new regulatory mechanisms. Increasing awareness of the needs of society and science will encourage interactions between scientists, policy makers and government in the development of appropriate regulatory frameworks, building on the structures already in place in the UK.

The same development of understanding of which genes may contribute to unwanted human characteristics, as well as to desired ones, will lead to pressure from some quarters to deliberately eliminate undesirable genes from an individual, and possibly to introduce desired ones. Such human genetic engineering is unlikely to be regarded by scientists as truly safe in ten years time. However, it is likely that society will have to address issues of the ethics of this and similar issues in preparation for the scientific possibilities, particularly as there are likely to be claims that such genetic manipulation can be achieved with fertilised human eggs.

Genomic sciences will greatly benefit if the links between society's wish and need for genomics and what the science can deliver are improved such that the science is in part responsive to the needs of society. This will increase the acceptability of advances made by genomic science, and help to resolve some of the reservations that the public has expressed in the past over such issues as genetically modified food and aspects of animal cloning.

### **4.4 Genomics and the wider world**

Genomic sciences will be driving many developments in the wider world in ten years time. New techniques will allow genomics to be applied to an ever wider range of environmentally important species within natural populations. Genomics will provide a better understanding of the interaction of physical, chemical and biological factors influencing life on Earth. This will allow improved prediction and management of a sustainable environment and the ecosystem services it provides. Ecosystem services are 'the benefits people obtain from ecosystems'. These include provisioning services such as food and water; regulating services such as regulation of floods, drought, land degradation, and disease; supporting services such as soil formation and nutrient cycling; and cultural services such as recreational, spiritual, religious, and other nonmaterial benefits.



Climate and other environmental changes make the need for this research more pressing. We will be able to understand and monitor how climate change impacts are felt from individual species to natural cycles on a global scale and how 'new' ecosystems will respond to disease and pollution. Such developing understanding will be very wide in application and is likely to contribute to international policies and agreements aimed at managing and sustaining the environment and biodiversity.

There are important emerging issues in the application of genomic approaches to healthcare in the developing world, such as accessibility to medicines, patient stratification and the impact of perceived human population variation. Many of these represent inequalities in healthcare for different societies that will need to be addressed.

The ethical frameworks for research, clinical practice, manufacture and industrial activity are not uniform throughout the world. Whilst diversity is inevitable, it will be valuable for a level of international agreement to be reached on some ethical issues so as to ensure that the science of genomics, and other fields, is not brought into disrepute, as this damages the public perception of safety and benefit.



# 5

## ► How is progress achieved?

If the UK is to maintain its excellent record in developing and applying genomic sciences in the next ten years, it will be necessary to ensure that:

- ▶ There is a sustained funding effort into basic genomic research and technology development
- ▶ Research on model organisms is enhanced by increasing inclusion of environmentally relevant and economically important organisms
- ▶ Interdisciplinary research is encouraged, with funding bodies supporting systems that enable this including ensuring that any future Research Assessment exercise recognises its importance
- ▶ Funding bodies co-operate and interact to ensure that research effort is leveraged as far as is possible and that necessary resource and infrastructure development is undertaken
- ▶ The major challenges are the same for all the Research Councils. High level coordination is needed regarding the basic technologies (miniaturisation and portability) and data management/ analysis
- ▶ Full use is made of the breadth of genomic and other resources available in the UK, including the NHS
- ▶ Interdisciplinary approaches are emphasised in the training of PhD students and beyond
- ▶ The UK as a prime location of choice for overseas undergraduate and postgraduate students is maintained
- ▶ The communication of science is spread to wider society, in particular focusing on pre-university education and training in order to address the decline in the UK science skills base
- ▶ Development of improved translational applications for research outputs through increased interaction between government and non-governmental organisations, industry and other key stakeholders in the public and private sectors
- ▶ A particular focus on the immense data generation, capture, storage, handling and curation needs that arise from genomics. These are critical for future efficiency and to safeguard competitiveness and need to be managed whilst maximising benefit from publicly funded activities
- ▶ Developing international collaborations whilst maintaining key competitiveness, with scientific advances being considered in an International Development context according to relevant government mandates.



# 6

## ► Conclusions

Genomics is not 'old technology', but continues to exist as an underpinning force for new and emerging scientific disciplines such as systems biology. The first exciting discovery phase in genomics has led us to reassess our preconceptions of the function of sequence information. The phenomenal technological advances that have taken place as a result of investment in this research have resulted in the accumulation of reference datasets describing individual plant and animal species, and UK funding agency support has facilitated sequencing and annotation activities both nationally and in contribution to global consortia.

There is now a great challenge to relate this information to biological problems beyond these reference datasets species. For this reason the UK must continue our investment in basic genomic research, but at the same time relate it to the benefits that this can have for the bio-economy. Basic science discoveries can address deliverables such as personalised medicine, understanding of disease mechanisms and the control of disease control in humans, livestock and wild animals, improvements in crops for sustainable agriculture (food security) and new uses for crops (e.g. bioenergy), and the impact that these developments will have on the environment. All this must be achieved with a clearer appreciation of the social impact of such advances.

Targetted investment by the Research Councils has resulted in genomics becoming successfully embedded in many facets of UK research. As detailed above, there are still many areas where progress needs to be achieved. The UK is well-placed to respond to these new challenges through its strengths in the genomics base and our high innovation capacity.

### ► UK Genomics resources

NERC Environmental Bioinformatics Centre (NEBC) <http://nebc.nox.ac.uk/>

MRC Functional Genomics Unit [www.mrcfgu.ox.ac.uk](http://www.mrcfgu.ox.ac.uk)

MRC Centre for Genomics and Global Health [www.cggh.ox.ac.uk](http://www.cggh.ox.ac.uk)

ERA-NET Plant Genomics <http://www.erapg.org/everyone>

BBSRC-funded Resources and Equipment <http://www.bbsrc.ac.uk/funding/facilities.html>

BBSRC Genome Analysis Centre <http://www.tgac.bbsrc.ac.uk/>

ESRC Centre for Genomics in Society <http://www.genomicsnetwork.ac.uk/egenis/>

ESRC Cesagen Centre <http://www.genomicsnetwork.ac.uk/cesagen/>

ESRC Science in Society Programme <http://www.sci-soc.net/SciSoc/>

Wellcome Trust Sanger Institute <http://www.sanger.ac.uk/>

UK Biobank <http://www.ukbiobank.ac.uk/>