

House of Lords Science and Technology Committee: Inquiry on Genomic Medicine**Response by the Wellcome Trust**

April 2008

SUMMARY

Genetics and genomics research is advancing at a rapid rate – leading to major breakthroughs in our understanding of the role of genes in a wide range of diseases. We believe that this research offers enormous potential for the development of new healthcare innovations over the coming decades.

The UK is a world leader in genetics research, and is ideally positioned to play a key role in delivering the vision of genomic medicine. In order to fully realise the resulting health and economic benefits, it will be vital that the Government develops the mechanisms and resources required to support this research and ensure its effective translation via the health service.

The key messages contained in our response are summarised below.

Key messages

- It is essential that UK funders (including Government, charities and industry) sustain investment in genetics and genomics research, and that their efforts are coordinated effectively. Continued international collaboration will also be vital to deliver genomics research and develop and sustain the underpinning data resources that it requires.
- We are deeply concerned that the long term sustainability of the European infrastructure that makes freely available the sequence and variation of the human genome and the genomes of many other species should be so heavily dependent on private philanthropic funding.
- In order to unravel the role of genetic, environmental and lifestyle factors in multi-factorial diseases, studies of large patient cohorts will be essential. The NHS provides a unique research resource – offering potential to link large-scale genomic data with information on health outcomes and responses to treatments captured in electronic patient records.
- Genomics research and its health applications raise significant ethical, legal and social issues, including key concerns relating to confidentiality and consent. The regulatory framework must achieve a suitable balance – ensuring a supportive environment for research and its translation for health benefit, whilst providing robust safeguards to address these issues.
- The Government must plan effectively for the implementation of genomic medicine in the health service. In particular, there is a need to establish mechanisms for evaluating the clinical effectiveness of genetic and genomic tests, and to significantly expand efforts to educate medical professionals throughout the health service on these technologies.
- Continued support for public engagement activities will be crucial in order to ensure that patients are equipped to understand genetic risk information, and to foster a supportive public environment that allows the healthcare benefits of genomic medicine to be realised.

INTRODUCTION

1. The Wellcome Trust¹ is pleased to have the opportunity to contribute to the Select Committee's inquiry on genomic medicine.
2. The Wellcome Trust is the largest charity in the UK. It funds innovative biomedical research, in the UK and internationally, spending around £650 million each year to support the brightest scientists with the best ideas. The Wellcome Trust supports public debate about biomedical research and its impact on health and wellbeing.
3. We are a major funder of genetics and genomics research – providing support through our grant funding programmes for outstanding scientists in the UK and overseas to take forward cutting edge genetics research and related technology development activities. For example, we fund the Wellcome Trust Centre for Human Genetics in Oxford, which undertakes a broad research programme to investigate genetic susceptibility to disease and to translate this knowledge into advances in healthcare.
4. We also support the Wellcome Trust Sanger Institute² in Hinxton, Cambridgeshire – one of the world's leading genomics research centres. The Sanger Institute played a key role in the international Human Genome Project, taking responsibility for producing one third of the genome sequence. Its current research programme focuses on large-scale studies of genetic variation to advance our understanding of gene function in health and disease. The Sanger Institute has submitted its own response to the Committee's inquiry.
5. Over recent years, we have supported several major initiatives – both at the Sanger Institute and elsewhere – that are developing key genomics research resources for the international research community. Several of these initiatives have been developed in partnership with other funders – including public sector, charitable and commercial sector organisations. Examples include the International HapMap Project, the Structural Genomics Consortium and the UK Biobank.
6. Through our Biomedical Ethics programme, we fund research to examine the ethical dimensions of biomedical science and healthcare - this has included several projects exploring issues arising from genetics and its healthcare application³. We also support a broad range of activity to engage the public in biomedical science and its implications for society. In 2008, we launched a special call for proposals for public engagement projects addressing the theme of genes and health⁴. In addition, we fund the Nuffield Council on Bioethics and the Genetic Interest Group.
7. Our detailed comments in response to the specific questions raised by the Committee follow below. This response was informed by expert inputs from several grant holders and members of our advisory committees. We would be pleased to provide further details on the issues highlighted in this response or on any of the Wellcome Trust's activities in this area on request.

RESPONSES TO CONSULTATION QUESTIONS

Policy framework

Questions

- Who is in charge of setting and reviewing policy in this area?
- Who provides scientific advice on policy development? Who monitors and anticipates potential scientific developments and their relevance to future policy? How effective are these mechanisms?
- Does the existing regulatory and advisory framework provide for optimal development and translation of new technologies? Are there any regulatory gaps?
- In what way is science and clinical policy decision-making informed by social, ethical and legal considerations?
- How does the framework compare internationally?

8. We consider that the Department of Health has the primary responsibility for setting policy in relation to the uptake of genomic medicine into the health service in England. Via the National Institute of Health Research (NIHR), it is also responsible for funding and coordinating research undertaken in the NHS, and for translating this research into improvements in health services. The health departments of the devolved administrations likewise have the primary role for most aspects of policy development in Scotland, Wales and Northern Ireland.
9. The Government's 2003 White Paper on Genetics ("Our inheritance, our future") announced a series of initiatives to develop genetic services in the NHS. We consider that the White Paper provides a useful foundation, but that further investment in, and expansion of these initiatives will be needed in order to ensure the NHS will be equipped to maximise the potential of advances in genomics for health benefit.
10. The Department for Innovation, Universities and Skills (DIUS) and UK Research Councils - primarily through the Medical Research Council (MRC) - also have a key policy roles in terms of allocating public funding for basic and applied genetics and genomics research. The new Office for Strategic Coordination of Health Research (OSCHR) will assist in enhancing the coordination of MRC and NIHR research activities, and ensuring their optimal translation into health policy and practice – both in the context of genetics and genomics, and more broadly.
11. Since 1999, the Human Genetics Commission (HGC) has served as the Government's dedicated advisory body on human genetics – with a remit to analyse current and potential future developments and to advise ministers on their healthcare impacts and ethical, legal and social implications. Over its lifetime to date, the HGC has delivered a large amount of valuable work in this regard. We believe that there remains a need for an advisory body of this type, and that the HGC should continue to fulfil this role. There may, however, be scope for the HGC to refine its terms of reference to provide greater focus for its work moving forwards.
12. A key function of the HGC is to gather and coordinate information from the diverse range of stakeholders that contribute to policy development on issues related to genetics and its healthcare application. It will be crucial that the HGC retains the capacity to consult widely and to balance the diverse range of opinions it receives. The key stakeholder groups include:
 - other statutory and non-statutory advisory bodies - including the Gene Therapy Advisory Committee, the Genetics and Insurance Committee and Human Fertilisation and Embryology Authority;
 - the National Institute for Health and Clinical Excellence (NICE) and the Medicines and Healthcare Products Regulatory Agency (MHRA);
 - the research community (academic and commercial sector) – including research funders, institutions and individual researchers;
 - public interest and advocacy groups;
 - professional societies – such as the Royal Society and Academy of Medical Sciences;
 - the Nuffield Council on Bioethics;
 - the medical and associated professions.
13. We recognise that advances in genetics are raising important ethical, legal and social implications which will need to be considered by regulators. We discuss many of these issues in our responses to the questions that follow, but the key concerns include:
 - providing robust safeguards to protect confidentiality of individuals, whilst maximising secure sharing of data for research – as rapid technological advances make identifiability of individuals from genomic information an increasingly significant risk;
 - determining the criteria through which genetic tests are licensed for use in the health service and establishing effective processes and guidance for the communication of genetic risk information to patients;

- ensuring equitable access to the health benefits of genomics – including managing risks that “orphan populations” will emerge and ensuring the benefits reach the world’s poor;
- safeguarding against risks of discrimination and stigmatisation on the basis of genetic information;
- addressing concerns relating to genetics, race and ethnicity.

14. It is our view that the current regulatory framework in relation to genetics is satisfactory. We believe that it should be possible to respond to these issues through the use of existing structures, and that there is no clear need for additional regulatory or advisory bodies at this stage. We consider that the overarching goal of the regulatory framework must be to maintain an appropriate balance – providing a conducive environment for genomics research and its translation to health benefits, whilst ensuring that appropriate safeguards are established.

15. In order to anticipate and examine these issues, there will be a continued need to support high quality research into the ethical, social and legal implications of genetics and genomics, and to ensure that the outcomes of this research are considered in policy development. It is also vital that work is progressed to engage the public in discussions on genomic medicine and the issues it raises for society, as an informed and supportive public will be essential if the health benefits are to be realised. The Wellcome Trust will continue to support such work through its biomedical ethics and public engagement funding schemes and other direct activities, furthering opportunities to work in partnership with others where appropriate.

16. It is also important to note that policy developments relating to genetics and genomics are necessarily taking place in a broader international context – with discussions at European Union, OECD and United Nations (UNESCO and WHO) level. The UK should continue to contribute actively to these international processes - ensuring the development of conducive frameworks for international collaboration; facilitating regulatory harmonisation; and creating global frameworks to maximise benefits of genomics for global health.

Research and scientific development

Questions

- What is the state of the science? What new developments are there? What is the rate of change?
- Who is taking the lead in the consideration and co-ordination of research and the development of new technologies?
- How effective is the policy and investment framework in supporting research in this area?
- How does research in the UK compare internationally? How much collaboration is there?
- What are the current research priorities?
- What is the role of industry? How much cross-sector collaboration takes place?

17. The fields of genetics and genomics are advancing at a rapid rate, and have revolutionised basic biological research. Following the culmination of the Human Genome Project (HGP), there have been profound advances in our understanding of the structure of the human genome and the connection between genes and diseases.

18. Through the Wellcome Trust Sanger Institute, the UK was able to play a leading role in the HGP. The Sanger Institute has continued to contribute to major international collaborative initiatives to further our fundamental knowledge of the genome and to characterise human genetic variation – key examples include:

- International HapMap Project – a partnership involving research centres in six countries to characterise markers of variation across the human genome (building on the work of the earlier SNP Consortium which identified sites of single nucleotide variation in the genome);
- Genome Structural Variation Consortium – a project to characterise copy-number variations across the human genome, a previously underestimated source of genome variation;

- ENCODE (Encyclopaedia of DNA elements)– an international initiative funded by the US National Institutes of Health to characterise functional elements in the human genome;
 - 1,000 Genomes Project – a new international initiative to characterise the genomes of 1,000 individuals from around the world in order to produce the most accurate map yet of human genetic variation.
19. Scientists from all over the world are utilising the information generated by the Human Genome Project and these subsequent initiatives to gain new insights into how genetic factors underpin disease processes. The Cancer Genome Project at the Sanger Institute (see **Box 1**) is an example of a major initiative of this type, which is systematically scanning the genome to identify genes that contribute to the development of human cancers.
 20. Recent years have also seen dramatic advances through genome-wide association studies in large patient cohorts – these are utilising our knowledge of the genome together with rapid advances in genotyping technologies to begin to identify genetic factors that contribute to the development of complex multi-factorial diseases. The Wellcome Trust Case Control Consortium (see **Box 2**) has been the largest such study to date.
 21. The results of the first phase of the Case Control Consortium illustrate the immense power of genome-wide association studies - providing vital new insights into the biological processes underpinning major diseases that would not have been possible using traditional approaches. It is crucial to emphasise, however, that our knowledge of the role of genetic factors in these diseases is still at a relatively early stage. Given that the total genetic contribution by most genetic factors is small, much more research is needed to characterise the ways in which particular factors influence risk or protection. Additional and larger studies are needed to understand how genetic factors interact with other genes and with the environment to underpin the development of these diseases.
 22. The UK Biobank⁵ will collect samples and medical information for 500,000 UK citizens between the ages of 40 and 69, will be an invaluable resource to investigate the interplay between genetic, environmental and lifestyle factors in common multi-factorial diseases, as well as the relationship between intervention and health outcomes. UK Biobank is funded in partnership between the Wellcome Trust, the MRC, the Department of Health, the Scottish Executive and the Northwest Regional Development Agency.
 23. It is vital not to overlook the contribution that advances in genomics could make in the area of infectious disease. The availability of pathogen genome data, combined with the genomes of their human and animal hosts and vector organisms, is enabling researchers to make significant advances in understanding how infectious agents interact with their host organisms to cause disease. This knowledge will enable the development of improved diagnostics, vaccines and therapeutics to combat these global killers, and the academic, clinical and commercial sectors will need to work together to develop and evaluate these tools.
 24. Overall, we consider that the UK is a world leader in genetics and genomics research. Continued investment in basic, clinical and applied research from governmental, charitable and commercial sector funders will be vital to build on these foundations, and ensure that the UK is able to realise the health and economic benefits of innovation in this area.
 25. As many of the initiatives described illustrate, extensive collaboration amongst research teams, both at a UK and international level, is already a key feature of research in this field. The challenges faced in understanding the genome mean that large-scale approaches are required, with coordination at a global level to maximise the effective use of research funds. These partnerships are being driven forward by the research community, with the support of funding agencies. The UK's involvement in such partnerships to date has been backed to a considerable extent through funding from the Wellcome Trust and other non-governmental sources. There might be scope for the MRC and other public funders to take a more proactive role in supporting these international initiatives.

Box 1 – The Cancer Genome Project⁶

The Cancer Genome Project was launched by the Wellcome Trust Sanger Institute in 2000 under the leadership of Mike Stratton. Its aim was to identify somatic mutations implicated in human cancer, by systematically comparing the genomes of cancer patients with the reference genome generated via the Human Genome Project.

In 2002, the project had an early success with the identification of the signalling molecule BRAF as an oncogene in human cancer. Mutations in the BRAF gene were found in 60 per cent of malignant melanomas, 10 per cent of colorectal cancers and 40 per cent of borderline ovarian cancers screened in the study. The group has subsequently identified a number of other genes – including ERB2, activating mutations for which were found in a proportion of lung cancers. These gene products form novel targets for cancer drug development, and programmes to identify small molecule inhibitors for both BRAF and ERB2 are being taken forward in partnership with academic and industry partners.

The group subsequently focused their search for cancer genes on the protein kinase family of cell signalling molecules. In a paper published in *Nature*⁷ in March 2007, the project announced the identification of 1,000 somatic mutations in 518 protein kinase genes in 210 diverse human cancers. The paper described significant variation in both the numbers and patterns of mutations across different cancers and suggested that a larger repertoire of genes are implicated in cancer than previously anticipated.

In taking forward its work, the group has developed key resources for the cancer research community – including the COSMIC database, which collates data on somatic mutation from the Cancer Genome Project and scientific literature. The project is also now being extended in the context of the International Cancer Genome Consortium – an international confederation, which includes the Wellcome Trust and the Sanger Institute, to identify the causative mutations underlying 50 cancers.

Box 2 – The Wellcome Trust Case Control Consortium⁸

The Wellcome Trust Case Control Consortium (WTCCC) brought together 50 leading research groups and 200 scientists from a range of UK institutions, supported by £9 million funding from the Wellcome Trust. It analysed DNA samples from 17,000 individuals across the UK to study seven common diseases (bipolar disorder, Crohn's disease, coronary heart disease, hypertension, rheumatoid arthritis and type I and type II diabetes) – in each case, comparing DNA samples from 2,000 patients for common genetic variations against a set of 3,000 control samples. The study analysed 500,000 markers of single base-pair variation (single nucleotide polymorphisms) across the human genome.

A series of major scientific publications were produced during 2007 from the first phase of the initiative. As well as confirming the involvement of some genes for which disease association had already been reported, the study also identified novel genes that affect susceptibility to these complex diseases. The major advances made by the WTCCC and other genome association studies was illustrated by its selection as *Science* magazine's 'breakthrough of the year' for 2007.

In 2007, the Wellcome Trust committed a follow-on award of £7.7 million to WTCCC to further investigate the genes it had identified and to characterise copy number variations. In April 2008, we announced a further £30 million in follow-up funding for a series of genome-wide association studies. Together these studies will analyse DNA samples from 120,000 people, enabling researchers to investigate 25 diseases, as well as supporting studies into the genetics of learning in children and individuals' response to statins.

26. The commercial sector has pivotal role to play in genomics research, and maximising collaboration between academia and industry will be vital to ensure the effective translation of research advances into new healthcare products and technologies. Furthermore, there are already strong examples of collaborative initiatives which have brought together public sector, charitable and industry funders to build key research resources for the benefit of both academic and commercial sector researchers. Examples include:

- the SNP Consortium – a partnership established in 1999 between the Wellcome Trust, 13 pharmaceutical and technological companies and sequencing centres in the UK and US to characterise sites of single base pair variation across the human genome;
- the Structural Genomics Consortium – an international collaboration supported by the Wellcome Trust, public sector funders in Canada and Sweden, and three pharmaceutical companies (GlaxoSmithKline, Merck and Novartis) for large-scale characterisation of protein structures;
- the Severe Adverse Events Consortium – a consortium with support and involvement from Novartis, Abbot Laboratories, Johnson and Johnson, GSK, Wyeth, Roche, Pfizer, Sanofi Aventis, Takeda, Daiichi-Sankyo and the Wellcome Trust, which is aiming to identify DNA-variants useful in the prediction of drug-induced serious adverse events – with the translational goal to improve patient safety and reduce morbidity related to adverse events.

Data use and interpretation

Questions

- Is genomic information published, annotated and presented in a useful way? Should there be a common, public database? If so, who should fund, and have responsibility for, such an initiative?
- Who should provide the framework for optimal evaluation of data and translational opportunities? What policy and funding mechanisms are in place for recognising and utilising potential opportunities?
- Is other medical information recorded in a suitable format to allow optimal interpretation of genomic data? How should genomic data be brought together with other health information?
- What are the implications of the generation and storage of genome data on personal data security and privacy, and on its potential use or abuse in employment and insurance? How should these be addressed?

27. The Human Genome Project set a new paradigm for sharing of research data in the life sciences – with the sequence information being placed in the public domain immediately, so that it was freely available to all without restriction. We believe as fundamental principle that genomic research data should be shared as widely as feasible in order to maximise their use for ultimate health benefit, subject to issues of consent and confidentiality of research participants (as explained further below) . We have actively promoted the development of data sharing policies in line with this principle for the major genomics research initiatives that we have supported.

28. There are established database resources and software tools in place to store and annotate genome sequence data in a form suitable for use by the research community. One key resource is the Ensembl genome browser, which has been developed in partnership between the European Molecular Biology Laboratory (EMBL) - European Bioinformatics Institute (EBI) and the Sanger Institute and is funded by the Wellcome Trust. It is vital that public funding agencies also provide long-term funding commitments to ensure that key research resources of this type are sustained. We are deeply concerned that the long term sustainability of the European infrastructure that makes freely available the sequence and variation of the human genome and the genomes of many other species should be so heavily dependent on private philanthropic funding.

29. The huge volumes of divergent data that are being generated by life sciences research in the genomic era continue to create demands for new, more powerful informatics resources and

platforms to enable researchers to share, analyse and interpret this information. Coordination at EU and international levels will be vital to build and sustain the data resources required to underpin this research, and to ensure the establishment of data standards that allow the comparison and integration of divergent datasets to maximise their use. It is crucial that the UK continues to contribute actively to these initiatives.

30. We support the EBI, which will have a vital role in this regard. The EBI is participating in the development of several major European-level initiatives to develop the data infrastructure needed to underpin life science research – including, for example, the ELIXIR (European Life Sciences Infrastructure for Biological Information) project. It is vital that the UK continues to advocate for long-term sustainable European Union funding for this key resource provider.
31. Whilst established resources exist for researchers, the provision of genomic data in a format suitable for use by clinicians is less well advanced. As genomics research advances and more clinically-relevant findings result, there will be a need for resources that collate and present information in a way that can support clinicians in their decision making. One example of an existing project is the DECIPHER (Database of Chromosomal Imbalance and Phenotype in Humans using Ensembl Resources) initiative at the Sanger Institute, which uses genomic array technologies to identify chromosome abnormalities in children with developmental defects and presents this alongside clinical information about chromosomal abnormality. Further support for the development of these types of tools, alongside the provision of education and guidance for clinicians (as highlighted below) will be crucial.
32. As highlighted above, unravelling the genetic, environmental and lifestyle factors that contribute to the development of complex multi-factorial diseases will require studies of large cohorts, which bring together genomic data with medical and lifestyle information. The UK Biobank will provide an invaluable resource to undertake this work. A current limitation in such studies is the lack of suitably robust systems to measure and record phenotypic information in a consistent format, and the development of new standards and formats for such data is required.
33. Building on this point, we believe that the medical information held by the NHS has enormous value as a research resource. There is considerable potential to utilise the information collected on electronic patient records in the context of these large-scale studies, and to develop systems for capturing phenotypic and lifestyle information in consistent and accurate formats. The Research Capacity Programme within the Connecting for Health initiative holds considerable promise in this regard. The Trust is funding a joint initiative in partnership with the MRC, EPSRC and ESRC to support the use of electronic patient records in research, and there will be considerable scope in the future to integrate genetic information with medical record information in these types of studies.
34. We suggest that Generation Scotland provides a good model of how NHS patient records can be harnessed in the context of translational medicine, and how large-scale genetics studies could be integrated alongside clinical genetics and associated public engagement activities. There might be strong potential for the system in England to adopt this more joined-up approach.
35. Whilst we believe that the opportunities to share genomic data should be maximised, it is vital that appropriate technical and regulatory safeguards exist to protect the confidentiality and security of personal information collected and used in research and healthcare practice. In the context of research, there are well-established mechanisms to de-identify data which can provide appropriate protections to safeguard the confidentiality of participants. We recognise that, as genotyping technologies advance and whole-genome sequencing becomes technologically feasible, it may become possible to identify individuals from genomic data. Although this is a hypothetical concern at this stage, it will be vital that the regulatory framework keeps pace with rapid technological developments in this area. There are also legitimate concerns regarding the use of genetic information in non-medical contexts – including insurance and employment, and appropriate regulatory provisions will likewise be required to address these concerns.

36. Another key issue in the context of research is that of informed consent. Individuals must be provided with sufficient information on how their data will be used in order to enable them to make an informed choice as to whether to participate in a particular research project. For the purposes of research, however, it is often desirable to attain broad consent so as to maximise the potential uses to which the data can be put and the resulting benefit that can potentially be gained. Balancing these requirements is a significant challenge in large-scale cohort studies.
37. The UK Biobank initiative has an Ethics and Governance Framework in place. This sets out the ethical standards guiding the project, and is widely seen as a 'gold standard' for population cohort studies. There is considerable potential to develop enhanced collaboration between the major cohort studies that are taking place in different countries in order to maximise the value of the data collected, and ensure the development of common best practice frameworks. The Public Population Project in Genomics (P3G) consortium⁹ aims to promote scientific interoperability and harmonization of regulatory frameworks between major cohort studies.

Translation

- What opportunities are there for diagnostics, therapeutics and prognostics - now and in the future?
- Who is responsible for translation to clinical practice?
- Given the pace of technological advance, how 'future-proof' is healthcare investment in this area?
- How does the UK compare to other countries and what lessons can be learnt?
- How meaningful are genetic tests which use genome variation data? What progress has been made in the regulation of such tests?

38. We consider that genomics research offers huge potential for the development of new and improved diagnostics, therapeutics and preventive approaches over the coming decades. The Department of Health has ultimate responsibility for ensuring that these innovations are taken up into health service, but the pharmaceutical and biotechnology sector will also have a key role in progressing the commercial development of new healthcare products and technologies.
39. It is our view that the translation of advances in genetics into clinical application will proceed gradually, and that new innovations will emerge incrementally in the majority of areas. Nonetheless, it is vital that the health service plans effectively and sets in place the systems required to ensure the effective uptake of clinically-useful technologies as they develop.
40. The impact of genomics on drug development pipelines has not as yet been as profound as many had predicted. The use of genomic technologies is, however, resulting in the identification of new potential targets, with potential to enable the development of new, more effective drug treatments in some therapeutic areas. One such area is cancer, and the identification of the BRAF target in the Cancer Genome Project (Box 1) provides an example of how genomics research can feed rapidly through into new drug development projects.
41. It is also likely that there will be a gradual emergence of new treatments that aim to combat disease through the alteration of gene function. Over the coming decade, some treatments based upon gene therapy approaches should enter clinical practice – most likely for either monogenic diseases or cancer. We are also likely to see the further development of more sophisticated gene silencing approaches, utilising the techniques of RNA interference (RNAi).
42. In terms of genetic testing, the main focus in the short term is likely to remain on tests for monogenic disorders, and rarer subsets of common diseases where a single gene has a major impact. Although much research remains to be done to identify the genetic factors that underpin multi-factorial diseases, it is likely that some clinically-useful tests to predict risk of diseases of this type will start to emerge over the coming years. In addition, ongoing rapid technological developments are likely to bring the cost of individual genotyping, and even whole genome sequencing, down to more cost-effective levels over the next decade.

43. The introduction of new genetic and genomic tests into healthcare practice will need to be based on a rigorous consideration of their power and the clinical utility, together with careful assessment of their cost-effectiveness; consideration of how the information generated will be communicated to, and used by, patients; and examination of wider ethical issues they raise. Because our understanding of genetic risk factors of common diseases is at a relatively early stage, further research is needed before information on genetic risk factors for these diseases will have value in a clinical setting.
44. Recent reports by the Human Genetic Commission¹⁰ and PHG Foundation¹¹ have highlighted the absence of a clear process for the clinical evaluation and regulatory approval of new genetic tests. We agree with their conclusions that this is an area which needs further attention. Significant concerns are also being raised about direct-to-consumer marketing of genetic tests. Regulation of companies offering such services constitutes a significant challenge, and will create a need to ensure that accurate and trusted sources of information are available to the public on the tests they provide.
45. Over the coming years, it is also likely that there will be a gradual emergence of pharmacogenetic tests, which aim to ensure prescription of the most efficient drug, or combination of drugs, based on a patient's genotype. These technologies could result in significant benefits both for patients and the health service - reducing unnecessary prescribing and the risk of adverse events. Advances in pharmacogenetics do, however, raise a series of ethical concerns – including the risk that sub-populations will develop for which no effective drug treatment exists for a particular disease. There are also important questions as to how new tests should be approved in the context of drug licensing and over the implications of possible market segmentation on drug development. The scientific and ethical issues associated with pharmacogenetics have been considered in detail in reports by the Royal Society¹² and Nuffield Council on Bioethics¹³.

Biomarkers and epidemiology

- In what way do genome-wide association studies contribute to the identification of biomarkers? How is the study of genetic factors and biomarkers integrated for translational purposes?
- What impact will genomic data have on data emerging from projects such as UK Biobank, Generation Scotland and other biobanks?

46. The potential identification and use of biomarkers is an area that is receiving considerable attention, and is likely to be accelerated by genome-wide association studies. However, a lot more basic research is needed to develop these studies and translate the knowledge generated into new biomarkers. As with genetic tests, effective systems will also need to be established for the clinical evaluation of tests based on biomarkers.
47. The availability of genomic data and that emerging from biobanks will provide a very powerful tool for researchers studying the various environmental and genetic factors at play in complex diseases. As indicated above, the UK is uniquely positioned to exploit the data emerging from the UK Biobank and in its ability to access patient data from the NHS to inform such studies.
48. Many of these issues are considered in more depth in the report of a joint European Union-Wellcome Trust meeting held in September 2005¹⁴. This meeting highlighted the importance of developing bio-resources and nation wide-registers to correlate genotype, phenotype and environmental information, and for closer coordination of biobank resources across Europe. The latter is being developed in the context of the EU Biobanks project, as part of the European Strategy Forum for Research Infrastructures (ESFRI).

Use of genomic information in a healthcare setting

- What impact will genomic information have on the classification of disease? How will it affect disease aetiology and diagnostic labels?
- How useful will genomic information be as part of individualised medical advice? What provisions are there for ensuring that the individual will be able to understand and manage genomic information, uncertainty and risk?
- Should there be a regulatory code (mandatory or voluntary) covering the provision of this advice?
- What are the implications of developments in genomic technologies for the training of medical specialists and other health professionals? Are there any gaps that need addressing? What is the assessment and planning for future needs in capacity?

49. It is likely that as our knowledge of the role of genes in diseases processes increases there will be new classifications of disease, as well as greater sub-classification of diseases, based on underlying genetic profiles. The hope is that this will ultimately enable preventive strategies and treatment options to be targeted more effectively based on the underlying genetic characteristics of the disease.
50. As our understanding of how genetic factors underpin complex diseases is still at a relatively early stage, it is likely to be some time before this vision is fully realised. As noted above, appropriate processes will need to be developed to evaluate genetic tests before they are provided on the health service in terms of their power, clinical value, cost implications and any broader ethical implications. There will be particular concerns in situations where no effective clinical intervention exists based on the outcomes of the genetic test.
51. It is likely that the provision of genomic and pharmacogenetic tests will in the future be provided at the point of primary care, rather than through specialist genetic services. There will also be an increasing number of patients who will seek advice from physicians based on results of direct-to-consumer genetic tests. There is, therefore, an urgent need to ensure that professionals across the health service are educated on genetics and the ethical and social issues it raises. They must also have access to accurate information on what genetic tests are available and the clinical implications of the results; and be able to accurately convey genetic risk information to patients. Access to specialist genetic counselling services will need to be provided where appropriate.
52. The 2003 Genetics White Paper and the Progress Review published in April 2008 recognise the importance of educating medical professionals in genetics. It is vital that initiatives in this area are expanded significantly. We also agree that there will be a need for development of clear clinical guidelines for the communication of genetic and genomic risk information.
53. It is expected that the availability of genomic information will ultimately provide the potential to target preventive public health interventions within the population – with the goal of encouraging those at particular risk of developing diseases to reduce lifestyle risk factors. Large questions remain, however, on the extent to which patients will act on risk information and adopt appropriate lifestyle interventions. We suggest that there is a pressing need for further research studies to examine how behavioural interventions can be successfully implemented, if genomic information is to be utilised effectively in a public health context.
54. As highlighted above, underpinning all of this is a need to ensure the public is appropriately informed and engaged on advances in genetics and genomics and the ethical and social questions they raise. The media and research community have vital roles to play in ensuring that this information is communicated in a balanced way in terms of the benefits and risks, and that the public have realistic expectations of genomics and its healthcare potential. As noted above, continued focus by Government and other funders on public engagement work should remain a core component of efforts to ensure the vision of genomic medicine is realised.

References

1. For further information on the Wellcome Trust, see our website: www.wellcome.ac.uk
2. For further information on the Wellcome Trust Sanger Institute and the activities described in this response, see: www.sanger.ac.uk
3. Descriptions of projects funded through our Biomedical Ethics programme that examine issues arising from genetics may be accessed on our website at: www.wellcome.ac.uk/Funding/Medical-humanities/Past-funding/Biomedical-ethics/Outputs/WTD003338.htm
4. See our Society Awards page (theme for these awards for 2008/09 is Genetics and Health): www.wellcome.ac.uk/Funding/Public-engagement/Grants/Society-Awards/index.htm
5. For further information on UK Biobank, see: www.ukbiobank.ac.uk
6. For more information on the Cancer Genome Project, see: www.sanger.ac.uk/genetics/CGP
7. Greenman et al: "Patterns of somatic mutation in human cancer genomes", Nature 446 (8 March 2007), p153-158
8. For further information on the Wellcome Trust Case Control Consortium, see: www.wtccc.org.uk
9. Further information on the Public Population Project in Genomics (P3G) can be found at: www.p3gconsortium.org
10. Human Genetics Commission (December 2007): *More Genes Direct*
11. PHG Foundation and Peninsula Medical School (February 2008): *Evidence and Evaluation: building public trust in genetic tests for common diseases.*
12. The Royal Society (September 2005): *Personalised medicines: hopes and fears*
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