

Cancer Research UK submission to the House of Lords' Science and Technology Select Committee sub-committee inquiry into Genomic Medicine

1. Summary of key points

1.1 Cancer Research UK recognises the significant potential genomic medicine presents, and welcomes the interest of the House of Lords in this area. However it is vitally important that the committee is clear in its definition of genomic medicine. Cancer Research UK defines genomic medicine as 'the use of genetic information to determine disease risk and predisposition, diagnosis, prognosis, and the selection and prioritisation of therapeutic options'. We strongly recommend that the Committee use a similar definition.

1.2 It is anticipated that genomic medicine will have a particularly significant impact in cancer. To expedite the introduction of genomic medicine Cancer Research UK recommends that:

- **through education and public debate, society is prepared for the introduction of genomic medicine in the NHS.**
 - The Government must work with the National Health Services and education systems across the UK to ensure that the UK is prepared for a future that embraces genomic medicine.
- **appropriate planning and training ensures that advances in genomic medicine are supported by an adequate medical workforce.**
 - The Higher Education sector together with professional groups, including the Royal Colleges, should lead the development of a genomic medicine-ready workforce.
- **regulation is in place to ensure that the public are able to benefit from the potential of genetic tests.**
 - The Government must develop and implement a regulatory framework with the support of the National Institute for Health and Clinical Excellence (NICE) and the Medicines and Healthcare products Regulatory Agency (MHRA).
- **researchers are able to use NHS resources, such as electronic health records, to advance our knowledge in this area.**
 - The Government must ensure that the regulatory framework governing research using patient data is supportive and incentivises research.

2. Introduction

2.1 Cancer Research UK¹ is the world's largest independent organisation dedicated to cancer research. We funded £315 million of research last year, supporting the work of more than 4,250 scientists, doctors and nurses in over 35 towns and cities across the UK. Cancer Research UK recognises the value and importance of genomic research and we fund a significant portfolio in this area. This has included major financial commitments over the last three years for genome wide-association studies, which aim to identify new risk factors for a number of common cancers including breast, prostate and colorectal.

¹ Registered charity no. 1089464

2.2 Cancer Research UK welcomes the opportunity to respond to this consultation. The consultation is very broad, and the Committee may wish to revisit the scope to give more clarity and direction to the review.

3. General Comments

3.1 The term 'genomic medicine' is broad and can be ambiguous. It is often used as a catch-all term to cover industrialised methods of data acquisition and analysis to improve medical care, including prognostics, diagnostics, preventive intervention, therapeutic selection, and individualised treatment based on the complex interaction between inherited and acquired elements of human variation. Further to this, in the case of cancer, it is often helpful and necessary to distinguish between genomic medicine in relation to inherited susceptibility to disease, and genomic medicine in relation to non-inherited, acquired (somatic), changes. It would be useful if the Committee could clarify how they are defining this term.

3.2 We would also like to take this opportunity to highlight the importance of the NHS to genomic medicine. The unique nature of the NHS should provide an enviable resource of well-annotated clinical material. We recognise that much has and is being done to ensure the availability of this type of material through the Research Capability Board (RCB), National Cancer Research Institute (NCRI), National Institute for Health Research (NIHR) and NHS R&D. However the Government must commit the necessary long-term resource if we are to gain the full potential from this type of research.

4. Policy Framework

4.1 There is no clear policy framework structure for genomic medicine. The Research Ethics Committees (RECs) and the Patient Information Advisory Group (PIAG) provide aspects of social, ethical and legal consideration for research in this area. However the role of these bodies is for prospective research applications and not with ethical issues involved in implementing the results of research.

4.2 It is often difficult to engage government in considering the how we can translate the results of research into practical clinical application. We would welcome a process to review research findings and consider how they might be implemented in conjunction with bodies such as the National Institute for Health and Clinical Excellence (NICE) and the Medicines and Healthcare products Regulatory Agency (MHRA). Any review body assigned this role should have representation from the laboratory and clinical staff from the NHS genetic diagnostic services as well as representatives from academic medicine, patients, and the public.

4.3 In addition, there is a need for a defined regulatory framework for the development, licensing and marketing of genetic tests to ensure that the public are not taken-advantage-of by unscrupulous companies.

5. Research and Scientific Development

Partnerships

5.1 This is an area with a significant amount of research and substantial collaboration both within academia and between academia and the pharmaceutical and biotech industries. An example of this is a collaboration between the Medical Research Council (MRC) and GlaxoSmithKline (GSK) to identify new therapeutic targets from

genetic association studies. More information can be found at <http://www.mrc.ac.uk/NewsViewsAndEvents/News/MRC004343>.

5.2 Collaboration between academic groups within and out with the UK is driving forward the development of new technologies and methodologies. One way this is achieved is through the sharing of reagents. However, the incorporation of these technological developments into academic science is often dependant on the availability of funding. International collaboration is often vital to the success of large studies where tissue samples from across the globe are required.

5.3 The NCRI plays a role in identifying areas that require research investment and in the strategic coordination of research activities of its member organisations. In parallel to this it is important for funding organisations to place value on research that could provide benefit in the longer term. We have some concerns that at times the Department of Health's (DH) calls for proposals place too much weight on studies aimed at short-term benefit, and that expectations of pharmacogenetics are somewhat overoptimistic.

Personalising healthcare

5.4 Given the interest in genomic medicine and the current rate of advancement in research it is likely that the determinants of susceptibility in inherited predisposition will be uncovered over the next decade. It will then be possible to give increasingly precise estimates of risk of different diseases to individuals. In recognition of this Cancer Research UK's Population and Behavioural Sciences Committee is funding work in this area exploring how preventive action can be tailored to individual genotype, the effect of genetic risk information on behaviour, and the psychosocial impact of detection of increased risk.

5.5 It may also be possible to predict the outcomes of disease, to the extent that these are determined by genetic factors. With regards to somatic genetics in cancer, it will be increasingly possible to distinguish between different molecular sub-types of cancer. In addition, genome-based determinants will play an increasing role in early diagnosis. In conjunction with the development of targeted treatments genetic information will facilitate the prediction of those therapies that are most likely to be effective in individual patients.

5.6 While pharmacogenetics may occasionally have applications where an identifiable genetic determinant confers a substantial risk of toxicity, insufficient attention has been paid to the constraints on the likely predictive value of common pharmacogenetic variation and whether it will be sufficient for practical clinical use. To this end more coordinated evaluation of research findings and of the potential use of new technologies by the NHS is needed.

Workforce

5.7 To ensure continued development in this area the Government must ensure that there is an adequate workforce, such as clinical pharmacogeneticists, trained to undertake and translate genomic medicine research.

6. Data Use and Interpretation

Annotation

6.1 Genomic medicine researchers generally make their research findings, including genomic data, publicly available in a quick and timely manner. It is important that any

genomic data is well annotated and we encourage our researchers to use the Human Genome Variation Society (HGVS) nomenclature (<http://www.hgvs.org>).

Databases

6.2 Compiling the genomic data generated by researchers into a common public database would have significant potential benefit. In order for databases to be useful there must be confidence that the data held is accurate and well annotated. With the advent of new high-throughput techniques there is a risk of large amounts of data being generated and included that due to technical errors is incorrect. Consequently there must be careful curation of any such database. This will also need significant resource and infrastructure support.

Data linkage

6.3 Genomic data is of greatest use when the information can be linked to the medical records. This has implications for confidentiality and access restrictions. The development of the new RECs Integrated Research Application System (IRAS) for research databases holds increasing potential of easier access and greater use of databases that contain additional patient information.

6.4 Linking genomic medicine data to health records requires the standardisation of clinical information such as in the electronic health record that all PCTs should be developing. We welcome the progress that Connecting for Health (CfH) and the Research Capability Board (RCB) have made in this area. However in order for us to realise the full potential of genomic medicine the Government must put the development of a national electronic health record at the top of its agenda. In addition to medical records, the disease registries, such as the national cancer registries, and the National Cancer Information Network (NCIN), play vital roles in collating such data.

6.5 The public anxiety around the use of 'personal information' must also be addressed if we are to be able to realise the full benefit of genomic medicine.

Clinical research opportunities

6.6 The opportunity that clinical trials present to genomic medicine should also be maximised. Cancer Research UK's Translational Research in Clinical Trials Committee (TRICC) funds translational research embedded in clinical studies such as the development of biomarkers.

Regulation

6.7 We also need balanced legislation to ensure that people do not suffer genetic discrimination based on the results of genetic tests. Examples of this is how genomic data is used when applying for life insurance, mortgages or jobs. Every individual should have the right to choose to take genetic tests free from the fear of future genetic discrimination. We welcome the current concordat and moratorium on Genetics and Insurance protecting patients against the use of genetic information by insurance companies but are concerned that a more permanent solution needs to be found.

6.8 Regulations or a mandatory code of practice should also be in place to ensure that the delivery of genetic information or test results is appropriate and takes into consideration the potential sensitivity of such information.

7. Translation

7.1 The potential that genomic medicine has for healthcare is vast. Although it is impossible to outline what all future opportunities will be, it is clear that genomics will revolutionise cancer medicine.

Developing genetic tests

7.2 Genetic tests that use genome variation data are in principle likely to provide a mechanism to discriminate between groups at substantially increased, or substantially lowered, risk of cancer. This discriminatory power will improve as more genome variation is discovered. However, it must be made clear that the power and utility of tests based on genome variation are likely to be dependant on risk estimates produced by combining the effect of all the known genome variants for a particular disease. Rarely will individual common variants have predictive utility. Regardless of this an increasing number of companies are developing and marketing predictive tests based on single genome variants. At times these are variants whose validity as risk markers is still unproven. The potential harm that these companies and tests can do is clear. The Government must ensure that these are appropriately regulated to protect the public from discrimination. Any regulatory framework must be sensitive to the behavioural and psychosocial impact that genetic information can have on an individual. Cancer Research UK is currently funding research in this area.

Supporting translation

7.3 Researchers, research organisations, the Government and industry must play their part in realising the promise of genomics. Individual researchers are responsible for developing and carrying out the proposals that will demonstrate the validity of translational applications. A successful example of how funders can work together to support such research is the Experimental Cancer Medicine Centres (ECMCs). The ECMCs are a joint initiative between Cancer Research UK and the Departments of Health for Scotland, England, Wales and Northern Ireland that provide the infrastructure and resource for translating research to develop clinical applications. The research community, industry and the Government must also consider how developments in genomic medicine should be validated, subjected to appropriate quality assurance and quality control testing and standardised. This should be supported by the development of clearer routes to incorporate research findings into clinical practice.

Workforce

7.4 The Government must also commit to addressing the workforce issues associated with translating this research and a future healthcare system that embraces genomic medicine. There is a requirement for more clinical academics, such as clinical pathologists, that are qualified to translate research findings. There is also a lack of clinicians across the specialities and professions allied to medicine who are equipped to deal with genomic applications. The detrimental potential of this should not be underestimated.

8. Biomarkers and Epidemiology

8.1 Biomarkers are key to translational research bridging basic and clinical cancer research. Biomarker methodologies allow hypotheses developed in the basic research environment to be tested in the clinical setting. Conversely, analyses of well-collected and annotated collections of clinical samples, particularly using large series and high-throughput technologies, allow hypothesis-generating research that can reveal new insights into cancer biology.

8.2 In addition to exploiting and informing basic cancer research, biomarkers are critical to decreasing cancer incidence and improving the lives of people who have cancer. The final stage of biomarker research is qualification, after which a biomarker or test can be used routinely in the general population or clinical setting. The development of qualified biomarkers are therefore central to many of Cancer Research UK's organisational objectives, specifically those that aim to reduce the risk of cancer, diagnose cancer earlier, develop better treatments and improve survival.

8.3 Although cancer research has for many years recognised the importance of developing new and more effective cancer treatments, the importance of biomarkers has not been fully appreciated or yet adequately supported. As cancer medicine moves towards the use of targeted therapies, biomarkers will become increasingly important because they:

- can help identify the best drugs faster;
- help to ensure that the right patients receive the right drug;
- provide 'proof of mechanism' for drugs in development;
- reduce late stage attrition and thus unnecessary cost by enabling those drugs that are likely to be suitable for final stage development to be identified earlier;
- support studies of optimal drug combinations;
- are key to proving whether existing agents could be used more effectively;
- accelerate drug approval by identifying robust correlates of outcome.

8.4 Consequently, biomarker discovery is complementary to drug discovery in the development of personalised medicine. However, there is currently no well defined structure for the biomarker development process to match that for the development of a new drug. Thus despite increasing investment in basic research to identify potential biomarkers and a demonstrable enthusiasm from clinicians for access to new biomarkers, the number of biomarkers that have been delivered into clinical practice is very small. There is therefore a pressing need in the UK and worldwide to develop paradigms for the discovery and development of biomarker assays and their translation into clinical practice.

Genome-wide association studies

8.5 Research activities such as genome-wide association studies have the potential to identify markers of individual risk of disease, of disease natural history, and of potential therapeutic or toxic response to therapy. Although findings from genome-wide association studies may impact on future clinical practice, this is still some years away and significant investment will be required to realise this potential. In particular investment is needed for:

- Large numbers (tens of thousands) of case and control samples to identify and validate risk factors with sufficient statistical power. For many diseases, sufficiently large sample sets can only be obtained through collaborative pooling of national and international resources. This is particularly an issue for rarer diseases where researchers will struggle to collect a sufficiently large number of samples.
- Sustainable infrastructure for collection, storage and maintenance of clinical samples and data.
- Research to identify whether the benefits of these genomic tests will be cost effective in comparison with current strategies for screening, diagnosis, prognosis etc. This is particularly important because studies looking at most of the genome variations identified confer only small differences in individual

risk, so many future clinical applications are likely to rely on combinations of markers.

8.6 Outcomes from genome-wide association studies will also help in the new identification of genes and pathways associated with disease risk, leading to greater mechanistic understanding and, eventually, new drug targets for prevention and treatment.

Biobanks

8.7 Biobanks have the potential to provide significant information on the link between genomic variation and the impact of lifestyle factors on health outcomes. However, it is unclear whether current biobanks are including sufficient numbers of people, such as the 100,000 participants in UK Biobank, to enable researchers to discern statistically valid information for a given specific disease indication.

9. Use of Genetic Information in a Healthcare Setting

9.1 Ultimately genomic medicine, through the acquisition of germline genomic and somatic genetic information, should allow the provision of individualised medical advice and treatment. Within the field of cancer this information should also enable the development of disease classification that is more biologically meaningful.

9.2 The NHS will need to have appropriate infrastructure in place to support the recording and cataloguing of somatic tumour genotype information collected by the cellular pathology diagnostic services.

9.3 This will also require understanding and acceptance of genomic medicine, and its implications by the public, politicians and the medical profession. One tool for addressing this would be through appropriate education of schoolchildren. The Government must also begin to consider the implications for workforce planning in the medical professions--such as the need for increased numbers of pathologists who can interpret and translate this information and genetics counsellors to provide support to patients. The Government should take immediate steps to address this.

9.4 Furthermore, given the potential implications of individualised medical advice, we believe that there is need for a regulatory code of practice for delivering genetic information or the results of genetic tests to patients, as discussed previously. This could stem from the national training scheme currently in place for genetic counselling. The mandatory code should be complementary to the rigorous processes determining the value and introduction of genetic tests from which the information to produce this medical advice will be determined.

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