CiS / CMF Day Conference
Technologies of the Future
October 2004

Which direction for the new genetics?

A gene for this and a gene for that, designer babies and bar-code babies are all ideas that are aired with increasing frequency in the media and represent both a general misunderstanding of what genes actually do and of the way in which genetic information may be used. So, what is the reality?

Human genetics has a much longer history than the human genome project. Indeed, indirect study of one particular human gene, that encoding ?-globin, has a special place in the history of molecular genetics. Further, many human genes had been identified before the HGP, including for example, those encoding the globins and that encoding the cystic fibrosis trans-membrane conductance regulator. However, there is no doubt that the coordinated effort to sequence the human genome has led to a greater understanding of human genetics and to our ability to utilise genetic information. The key question for society is how will that information be used.

Tests for many of the more common 'genetic diseases' are already available and can be applied at any stage of life, from the pre-implantation embryo created by IVF, the foetus in an established pregnancy, the new-born, the child and the fully-grown adult. Each of these situations presents its own dilemmas. For what conditions might pre-implantation genetic diagnosis (PGD) be sought? Is it acceptable to use PGD to create saviour siblings? If foetuses are tested, which conditions are serious enough to consider termination of pregnancy? What of informative tests for conditions for which there is no effective treatment? How should we use information about carrier status? The list of questions could go on but these give a flavour of the range of medical and ethical issues that are raised. Further, the available information will become much more extensive as the research effort on single-nucleotide polymorphisms is increased. This is leading to more extensive knowledge of the mutations that may cause genetic disease and/or to susceptibility to disease. Current research aims to apply this knowledge to the design of individual therapies, including drug therapies, based on a person's genetic makeup. This will require the ability to test for many polymorphisms in one go, for example through multiplex PCR, and eventually through microarray technology. This may not be a bar-code but perhaps a printout of a newborn's genetic susceptibilities is not so far away after all.

This leads on to developments of genetic intervention rather more subtle than, for example, termination of a pregnancy when the foetus has been diagnosed as having a serious genetic condition. PGD as part of IVF is already on offer for couples at risk of conceiving a child who is homozygous for certain recessive conditions and the availability of this will increase. PGD can also, as illustrated by recent cases, be used to select for characters which do not threaten the child to be born but instead will benefit a pre-existing sibling, for example by ensuring that the new baby is immunologically compatible with its older sibling in order to be a stem cell donor. And if we can apply PGD to selection for or against particular conditions, might we not also use it to select for or against features such as eye-colour?

The interventions so far mentioned do not involve actual genetic modification. However, direct genetic modification has been with us for some years now, in the form of somatic cell gene therapy, and although its success has been very limited, research is likely to continue. Germ-line gene therapy where the mutated gene is corrected in a heritable manner, is currently not permitted under the terms of the HFE Act. It is nevertheless possible to envisage situations in which such intervention is the only way that a couple could have child of their own (i.e. not adopted) who was free from a particular genetic condition. Even then it should be noted that the variation in the level of expression of the added gene(s) makes this a very uncertain procedure.

This leads on to consideration of using genetic modification to enhance in some way the child to be born. As ably described in print by one of our other speakers today, Robert Song, it may be difficult to distinguish between therapy and enhancement. However, assuming that this distinction can be made it is probable that in countries with less clear regulation than the UK, there may be pressure for genetic enhancement. Even so, it must be noted that, for the foreseeable future, any

couple wishing to undertake genetic enhancement of an embryo would need to be highly motivated to do so, seeing that involves all the procedures of IVF coupled with all the uncertainties inherent in the genetic modification of complex organisms.

In addition to the ethical dilemmas posed by the directly medical or biological application of human genetic knowledge, there are several broader issues that are raised. Will widespread use of genetic diagnosis narrow our perception of normality or even engender eugenic attitudes? Will there be widespread discrimination on genetic grounds in insurance or employment, even to the extent of creating a genetic underclass? And, finally, returning to medicine, will there be too much emphasis on genetics, turning people into bags of genes as if to imply 'the genes have spoken, there is nothing else to say.'

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