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The human genome

by Caroline Berry

In June 2000 scientists in America and the UK announced that they had completed the first rough draft of the human genetic code. Although it may be several years before the information is fully available for use by the scientific and medical communities, the next decades will probably see an explosion in the number of techniques that become available based on this research. As a society and as individuals we need to think fast so that we make good use of this phenomenal resource.

Four molecules (bases), adenine (A), thymine (T), guanine (G), and cytosine (C) 'spell out' the genes on which all living things are built. While viruses only have around 200,000 bases, human beings have three thousand million. Surprisingly about 90 per cent of this seems to be inactive. The rest forms the sequence for the 50-100,000 genes.

Genes give instructions that enable cells to build proteins. Errors in a gene's code can result in a faulty or absent protein. This can cause specific diseases or malformations, or it can increase a person's risk of succumbing to different illnesses. Changes in other genes are harmless and account for much individual variation. Some changes even protect individuals from certain diseases.

While microscopes have enabled scientists to understand how micro-organisms and viruses cause disease, the science of molecular pathology is enabling us to define the molecular changes that occur in cells when we fall victim to disease.

Clinical geneticists have already seen major changes in the quality of advice that they can give to families who seek their advice. During the next couple of decades, other specialities will feel the impact of these advances.

Current applications

Many single gene disorders have had their molecular errors identified and where these are straightforward, relatively simple diagnostic tests can be developed.

For example, doctors can confirm that a boy has Duchenne muscular dystrophy by looking for specific genetic changes in cells collected in a simple blood sample. This avoids the need for an invasive muscle biopsy. In addition, his mother, aunts and sisters can be told whether they are carriers of the disease. For those who request it, there is also an accurate early pre-natal test. None of this was possible before the development of molecular testing.

In another situation a family may find that some of its members have the mutation responsible for Hereditary Non-Polyposis Colon Carcinoma (HNPCC). Genetic tests can distinguish those who do or do not have the mutation. Those now known to be at a real risk are more motivated to attend monitoring sessions and resources can then be concentrated on them. At the same time, those without the mutation can be reassured and told that they do not need to be monitored.

Molecular diagnostic tests are also being used for classifying tumours and micro-organisms.

Potential new therapies

Replacing non-functional with functional genes in order to treat rare single gene disorders is the dream of gene therapy. However this is likely to take at least a few decades before it becomes established.

Doctors have had limited success in using gene therapy to treat a few children who have severe immunodeficiency. The treatment is possible because they take some cells out of the patient, add a new gene to these cells and then return them.

With other diseases, such as cystic fibrosis, there are enormous problems associated with getting new genes to the target cells.

More progress has been made in genetically manipulating bacteria, yeast and mammals so that they

produce valuable human proteins.

The bacterial production of growth hormone, however, illustrates that this can introduce new dilemmas as well as benefits. Because manufactured growth hormone does not carry the risk of being contaminated with the agent that causes Creutzfeldt-Jakob Disease, some parents of naturally short children are now asking for the hormone to 'enhance' their child's growth.

More tests

Attention is increasingly turning to common disorders such as asthma, hypertension and diabetes. All of these have a definite but complex genetic component. Researchers predict that there will probably be about 10 million normal variants within the human genome, some 200,000 of which will probably have some functional significance.

A striking example is new variant Creutzfeldt-Jakob Disease. Scientists believe that the disease is acquired from cattle with bovine spongiform encephalopathy (BSE). Everyone builds prion proteins (PrP) in their brains and normal PrP does no harm. But so far, only people with a particular common variant of the code at codon 129 on each of their two PrP genes have developed the disease.

People with one version of the code in both of a person's genes for apolipoprotein E are at a greater risk than others of developing Alzheimer's disease. The link is not strong, but in the future it could become one of a handful of genes that make up a highly predictive assay.

Also, prior to starting any drug treatment, a person's genetic profile might indicate which type of medication is most likely to succeed and which avoided because of genetic predisposition to side effects. For example, a person's response to medication commonly used to treat asthma is strongly influenced by a single base change in the gene that builds the drug's receptor.

There are many other examples of this phenomenon, so it is easy to see why the pharmaceutical companies are pouring money into genome research.

Dangers of genetic tests

Simple diagnostic tests that seek to find out what is wrong in people who already know they are unwell are non-controversial. But when apparently healthy individuals are tested more thought is needed.

the next generation

Healthy people may be tested to see if they are at risk of having a child with a genetic disorder e.g. cystic fibrosis or, in the Jewish community, Tay Sachs disease.

Advantages of such knowledge include being able to make informed decisions about child bearing, prenatal diagnosis or other options such as adoption. But it would be disastrous if testing, or even worse if prenatal detection and abortion, became compulsory or were driven by strong social pressure.

viewing your future

Finding out what you might be affected by at some time in the future has benefits and detriments.

People who find that they are at increased risk of diseases such as HNPCC can take steps to reduce their risk by careful surveillance and early surgery. On the other hand, testing for breast cancer genes is less satisfactory as current preventive measures are not always effective.

With other disorders, such as Huntington's disease, there is no treatment or means of preventing the disease. Consequently many at risk individuals prefer not to know.

In all these situations individuals are vulnerable to mental stress and depression. If the tests point to some risk, they may feel themselves undesirable as a marriage partner and have low self-esteem. They may also face the risk of stigmatisation and discrimination by employers, and insurance companies.

Everyone considering testing should receive careful counselling before starting any test.

Potential hazards

The scenarios described above are relatively straightforward and can be handled by awareness and sensitive pre-test counselling, but what of future developments?

We are already starting to identify genes and chromosomal regions associated with mental development, mental illness and personality traits. For example, children with William's syndrome have good social skills and enjoy company despite their learning difficulty. We now know that these children lack a small region of chromosome 7 indicating that genes in this area influence behaviour.

Discovering the genetic basis for some of our personal and mental characteristics could cause us to become reductionist and see ourselves as completely controlled by our predetermined genetic make-up. Alternatively it could lead us to have a fatalistic outlook on life, particularly by those whose genetic make-up seems far less than optimal.

With increased understanding of the genetic basis of disease and general characteristics such as height and intelligence, it might become possible to check for the genes in fertilised eggs, or even sperm and unfertilised eggs. This would give the ability deliberately to choose desirable or avoid undesirable

characteristics. This is the concept of 'designer children'. It is not feasible at the moment, but we need to be aware of the possibility.

More imminent is the possible use of genetically produced supplements to 'improve' healthy children. We need to distinguish carefully between treating sick people and 'enhancing' healthy ones. On occasions the dividing line will be unclear.

Finally, we have the spectre of 'genetic cleansing' and an increasing intolerance by society of those with genetic imperfections. We must remember that we all have genetically-determined risk factors but in our current state of knowledge only some are known. Most remain hidden. Many diseases are multifactorial and don't depend only on our genes.

The danger is that as a society we may decide that some imperfections are more undesirable than others.

A Christian response

These are new developments and ours is the first generation to be faced with making decisions on what is an appropriate use of the technology, what should be permitted and what banned. But in spite of the newness of the problems we do have fundamental and timeless principles that we can apply. They include:

1. truth and integrity

Both are basic to all forms of human interaction including medicine. All of us need to avoid exaggerated claims for our point of view or research project. Genetic research is too often reported in extreme terms that are not fully justifiable. This is due partly to biased reporting in popular media and partly to extreme comments from scientists and investors.

A vicious cycle of deceit is too easily set up. Governments and those advising them need to develop open and honest policies. Currently, official pronouncements are often greeted with cynicism, because once a cycle of distrust is set up it is difficult to reverse.

2. value and dignity

Some scientists, such as Richard Dawkins, maintain that we human beings are simply vehicles used by our DNA to get itself transmitted to the next generation. But there are many aspects of our humanity which indicate that we are much more than the sum of our genes.

We do not yet understand how our self-consciousness arises or the basis of our emotional life and artistic appreciation. It is possible to explain some forms of altruism by kin selection but not all altruistic acts involve family members and the capacity for self-sacrifice and concern for other people is very much part of our humanity.

The Creation stories in the first three chapters of Genesis show that we are each created in God's image. God is Spirit, he has no genetic code. Being in his image means we are much more than the sum of our genes.

Genes can perhaps be regarded as 'the dust of the earth' into which God breathed to make us the 'living beings' that we are. Being made in his image gives us free-will and the ability to make choices as did Adam and Eve in the Garden.

Our genetic make-up may determine which choices we find hard, but does not deprive us of the responsibility to choose good rather than evil. To assume that we are 'nothing but' our genes is reductionist and takes away from the dignity inherent in those made in God's image.

3. role of family

Currently our society overvalues the individual's autonomy and Christian affirmation of the family comes as a healthy corrective. Scripture shows us consistently that the family is the place where children are to be nurtured and valued for themselves as gifts to be cherished, not as 'products' for parental enjoyment.

As genetic influences affect more of medicine we will need to consider the family as a whole rather than just the individual. We receive our genes from our parents, we share them with our siblings and pass them to our children. To whom then do they belong?

When a mutation is found in one family member there are implications for many others. How this is handled tends to depend on the strength of the family's relationships. Those with strong bonds tend to cope with the difficulties of sharing hard facts about newly-diagnosed genetic disease, while those with poor relationships may refuse to pass on important knowledge. This gives rise to difficult issues of confidentiality and 'the right to know' versus 'the right not to know'.

Responsibilities are a better motive than rights, and care for each family member should be the guide as to how and who should be made aware of the need for genetic tests. But in real life these situations can be very difficult.

Ideally medical information should be kept confidential and never released without the consent of the person concerned. However, it may not always be easy to obtain that consent. For example a young pregnant woman who has a brother with muscular dystrophy may want to know her carrier status. An accurate test for her may depend on knowing the mutation present in her brother. She may not wish him to know of her pregnancy or that she is worried about having a child with his disorder. Should the geneticist obtain the boy's mutation result without his consent? And what if the brother is approached and refuses to let the information be released as he is concerned that his sister might want a pre-natal test and he is opposed to abortion? Does he have a duty to help his sister or is the life

of the fetus his rightful priority?

Weighing the pros and cons of informing a family member of their risk is not easy. Where preventive action is possible, knowledge seems beneficial despite the worry that the news may bring. With untreatable diseases such as Huntington's, however, some parents may wish to protect even their adult children from knowledge that they are at risk.

Once the matter has been raised, life can never be quite the same again. Costs and benefits must be explained carefully in the genetic counselling clinic, but there is currently no way by which family members can be forced to pass on genetic information.

testing minors

Do parents have a right to know their child's genetic make-up and have him or her tested in childhood, or should the child be protected from parental inquisitiveness (often laden with anxiety and even guilt) and allowed to make their own decisions as adulthood approaches?

It is difficult for parents of young children to remember that their offspring will grow up into independent adults who may decide they do not want to know their status, or may prefer to postpone testing until they are established in a relationship or about to start a family.

Where childhood testing offers no practical benefit it should usually be postponed and most parents see the sense of this after discussion. Testing may also be requested by adoption and similar agencies and again careful weighing up of both the short and long term interests of all concerned is essential, with those of the child having priority.

4. justice for the weak

Christians have a special responsibility to care for disadvantaged people. We need to protect the 'genetically weak' with regard to employment, financial security, mortgages etc, and from adverse public opinion.

We need to be aware of the huge commercial pressures building up around the provision of genetic tests and the possibility of people being persuaded to be tested without the necessary thought beforehand. This will become particularly acute if genetic tests become commercially available on an over-the-counter basis and this trend should be resisted, certainly for now.

Patenting enables inventors to benefit financially from their discovery. Biotechnology companies claim that they need this so that they can profit from their investments and generate new revenue for further research. But the patenting of DNA sequences whose function was unknown is now recognised as unreasonable. European Union legislation is in progress but the balance of interests is difficult and fair solutions need to be found.

Commercial exploitation plus the high cost of tests means that some can't afford them. This inequality is already with us as only Western style medical services can access genetic tests. Is it right to spend so much on these new developments while people in less favoured parts of the world go hungry and children die for lack of simple vaccines?

Conclusions

These four guiding principles give us signposts, but we will still have difficult decisions to face when they come into conflict with one another and priorities have to be decided. Those drawing up legislation in particular need insight and wisdom.

Francis Collins is Director of the National Genome Research Institute of the USA. He is a committed Christian and spoke at a recent conference of Christians in Science, saying that Christians should marvel at the elegance and beauty of the genome and pray for a resurgence of faith in the scientific and medical communities. Without this he found it difficult to see how we are going to negotiate these troubled waters.

Further reading

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