

Gene therapy

Gene therapy targets the faulty genes responsible for genetic diseases. Inheriting a faulty (mutated) gene can directly cause a wide range of disorders such as cystic fibrosis and haemophilia. It can also cause susceptibility to some cancers. Gene therapy can be used to replace a faulty gene with a healthy version or to introduce a new gene that can cure a condition or modify its effects.

This type of gene therapy is called 'therapeutic gene therapy' or 'the use of genes as medicine'. It is an experimental form of treatment that is still in its infancy but has the potential to revolutionise treatment for all kinds of genetic diseases.

Gene therapy targets faulty genes

Genes are the blueprint for our bodies, governing factors such as growth, development and functioning. A genetic mutation means that a gene contains a change or 'spelling mistake' that disrupts the gene message. This makes the gene faulty. A mutation can occur spontaneously or may be inherited. Gene therapy aims to get rid of genetic diseases at their source by targeting the faulty gene.

The gene therapy process

The basic steps of gene therapy include:

- The faulty gene that causes a specific disease must be identified.
- The location of the affected cells must be pinpointed.
- A healthy version of the gene must be available.
- The healthy gene has to be delivered to the cell.

A range of delivery techniques

The current problem is to find a way to successfully 'deliver' the new gene. To begin with, the affected cells are taken from the person's body and the correct genetic information is either 'spliced' or injected into these cells. They are left to grow in the laboratory and then replaced into the person.

One promising technique is to put the healthy gene inside a harmless virus, which has had most of its own genes removed (has been 'deactivated'). A virus that causes disease (such as the common cold) works by slipping into a cell, taking over its DNA and forcing it to produce more viruses. A deactivated virus can enter the specific cell and deliver the healthy gene.

Other techniques involve using stem cells. These are immature cells that have the potential to develop into cells with different functions. In this technique, stem cells are manipulated in the laboratory to accept new genes that can then change their behaviour. For example, a gene might be inserted into a stem cell that could make it better able to survive chemotherapy. This would be of assistance to those patients who could benefit from further chemotherapy following stem cell transplantation.

Adenosine deaminase deficiency

A person born with adenosine deaminase (ADA) deficiency lacks an important enzyme of their immune system. This means that infections are likely and can even be fatal. ADA deficiency was the first genetic disorder to undergo experimental gene therapy trials in 1990. It was chosen because a single, relatively uncomplicated gene causes it. The results were promising.

Bolstering the immune system

Current research is focusing on the immune system, which is a collection of special cells and chemicals that fight infection. If the immune system isn't functioning in the right way, illness can result. One theory on cancer suggests that the immune system is failing to stop the overgrowth of cells that form a tumour. If the immune system could be 'bolstered' with gene therapy, perhaps the body would be able to prevent the spread of cancer by itself. One day, gene therapy may also be used as a form of immunisation against particular infections, such as HIV/AIDS and malaria.

X-SCID

Another condition where gene therapy is promising is called X-linked severe combined immune deficiency (X-SCID). Children affected by X-SCID have a faulty gene that means they have no working immune system, so their bodies cannot fight infections. Only boys are affected due to the pattern of inheritance of the faulty gene.

Until recently, boys with X-SCID faced a lifetime living in a sterile bubble unless they could be given a matched bone marrow transplant. With gene therapy, bone marrow from the boy is first removed to 'harvest' stem cells. The stem cells are then infected with a virus carrying a working copy of the X-SCID gene, before returning the cells to the boy's body.

This treatment was described in 2000. Seven out of 10 infants treated to date have restored immune function but two of the children treated initially have developed a form of leukaemia. The leukaemia in these two patients was caused when the virus used to deliver the therapeutic gene activated a cancer-causing gene. After the first boy developed leukaemia in October 2002 and the second in January 2003, clinical trials of the gene therapy being conducted in a number of countries were halted. These have now been resumed but only for patients with no other treatment options. Work is continuing to make the therapy as safe as possible.

Body cells versus reproductive cells

A replaced, healthy gene would cure the individual. It would not prevent their children from inheriting the original faulty gene, however, as these are carried on the sperm and egg cells (called 'germ' cells). While the body's other cells (called 'somatic' cells) would have the updated healthy gene, the germ cells would still contain the defective one.

To make sure that future generations of the person's family were healthy, their germ cells would need to undergo gene therapy too. However, a complicated range of ethical issues, as well as technical problems, means that gene therapy of germ cells is only a remote possibility.

The risks of gene therapy

Some of these risks may include:

- The immune system may respond to the healthy gene copy that has been inserted and cause inflammation.
- The healthy gene might be slotted into the wrong spot.
- The healthy gene might produce too much of the missing enzyme or protein, causing other health problems.
- Other genes may be accidentally delivered to the cell.
- The deactivated virus might target other cells as well as the intended cells.
- The deactivated virus may be contagious.

More research is needed

At the present time, gene therapy is an experimental discipline and much research remains to be done before this approach to the treatment of disease will realise its full potential. Between 1989 and 2008, 1472 clinical gene therapy trials were initiated or approved worldwide. So far, less than one per cent of these have shown clinical benefit. The majority of the trials are being conducted in the United States and Europe, with only a modest number initiated in other countries, including Australia. The majority of trials focus on treating acquired diseases, such as cancer and AIDS, although an increasing number of inherited conditions are being targeted.

Ethics, morals and genetic engineering

Gene therapy offers a range of complex ethical and moral dilemmas. Some people believe that gene therapy is the same thing as genetic engineering. Currently, genetic engineering is concerned with altering food crops, while gene therapy aims to eliminate disease at its source, not produce a 'better' class of human being.

The concern is that manipulating factors such as intelligence might be tried, once gene therapy becomes commonplace. 'Ordinary' characteristics, such as shortness or average IQ, might then be considered as 'subnormal'.

Another concern is that gene therapy might only be available to the rich. The challenge for nations experimenting with gene therapy is to come up with workable, fair and ethical guidelines for its use.

Where to get help

- Your doctor
- Genetic Health Services Victoria, Royal Children's Hospital Tel. (03) 8341 6200

Things to remember

- Gene therapy is an experimental form of treatment. It works by replacing a faulty disease-causing gene with a healthy version or by introducing a new gene to cure a condition or modify its effects.
- The aim is to eliminate genetic diseases at their source.
- The challenge for nations experimenting with gene therapy is to come up with workable, fair and ethical guidelines for its use.

This page has been produced in consultation with, and approved by:

Centre for Genetics Education The

Copyright © 1999/2009 State of Victoria. Reproduced from the Better Health Channel (www.betterhealth.vic.gov.au) at no cost with permission of the Victorian Minister for Health. Unauthorised reproduction and other uses comprised in the copyright are prohibited without permission.

- This Better Health Channel fact sheet has passed through a rigorous approval process. For the latest updates and more information visit www.betterhealth.vic.gov.au.