Silencing the genes

A surprising number of diseases are caused by problems in our genes. Now we have unravelled the sequence of the human genome, more and more such diseases are likely to be discovered. Genetic modification has opened the door to the idea that we might be able to cure or prevent these diseases by changing the very nature of our genes.

Much of the discussion about gene therapy involves the idea of replacing damaged genes with healthy ones which will code for the right protein in the right place. However, a new and rather different approach, which may be very effective for some genetic disorders, is the idea of gene silencing.

Gene silencing is a very new technique, only invented in the late 1990s. As a result of silencing, specific genes can be shut down so that they no longer produce a rogue protein. The silencing is brought about by preventing the expression of the gene.

Scientists have found that by injecting nematode worms with a double-stranded piece of RNA which corresponds to a particular gene, they can block its action. They have even been able to feed the RNA to the worms and show that it has the same effect.

From worms to people is a big leap, but scientists have found that small chunks of double-stranded RNA can indeed block the action of genes in human cells as can short bent pieces of RNA. Short hairpin activated gene silencing (or SHAGging, as the researcher called it!) worked to prevent the production of certain proteins in lots of different types of cells.

The next step is almost the most exciting. Researchers have managed to genetically modify cells so that they code for engineered short hairpin RNAs. This means they have created cells which produce their own gene silencing mechanism. What is more, these cells can pass this engineered ability on to their daughter cells as the cell culture grows and divides.

The potential for this in the treatment of diseases like cancer and AIDS is enormous. But it is for genetic problems such as Huntington’s disease that gene silencing offers the most immediate hope of effective treatment.

The genetic mutation which causes Huntington’s disease results in the cells making too much of a specific protein, and it is this which causes the symptoms of the disease. Scientists in the US have been able to silence this gene in mice using gene therapy. It will be impossible to silence the gene completely in people, because brain cells cannot survive without the normal amount of the protein. However, affected people usually have one normal allele and one allele for the condition. If the affected allele can be silenced, leaving the normal allele working, then the symptoms of Huntington’s disease could be prevented.