

## Genetic Code and Designer Drugs?

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But scientists disagree on how soon their goal can be reached. First, they will seek to annotate individual genes in the DNA sequences and use these genes' products as targets for the development of new medicines. This strategy is new. So far, drugs have generally been developed by trial and error. In the huge arsenal of substances from the laboratories of synthetic chemistry and the treasure house of nature, scientists have searched for agents that happen, for example, to inhibit cell division and thus look like promising treatments for cancer. The high failure rate has driven the cost of developing a drug up to \$2 billion and more.

The Human Genome Project which has been underway for the last ten years, has held the promise of providing drugs that apart from providing cures for cystic fibrosis and other genetic disorders, could also treat more common diseases like cancer, cardio-vascular diseases, Alzheimer's and rheumatism by treating the underlying causes of these diseases. Now that we have the genetic information available as at least a working draft, if not the final proof, the situation does not look as straightforward as one had hoped.

faster and cheaper production of new and better drugs based on genetic information. They want to use the products of the genes, mainly cellular proteins, as pattern structures from which they can tailor medicines. It is a disturbance in the interplay of cellular proteins that causes disease. Once scientists have identified a gene and what it is producing that causes an illness, they can try to establish the three-dimensional structure of the protein. With this model, they can then computer-design chemical substances to replace, activate or inhibit the diseased protein or put it into the right shape.

Drugs developed using this method is already in use. They include the protease inhibitor to treat HIV infections and the neuraminidase inhibitor to combat influenza. These drugs were developed with virus target structures. But drugs designed specifically for cellular structures are also being tested. One of these is the inhibitor for an enzyme responsible for the overactive division of certain white blood cells. This promises important progress in the treatment of certain types of leukaemia.

But healthy skepticism is called for, particularly where proteins embedded in cell membranes are concerned. While these make particularly suitable target structures for drugs, their three-dimensional structure is difficult to determine. However, drug production will be speeded up by the new possibility of better understanding what happens inside the cells. By identifying all the proteins formed in a cell, researchers can draw up activity profiles under different conditions. A comparison of the protein profile of cells that have been treated with a certain drug and of cells that have not been treated gives clues on the effects that the drug has, for example, on the metabolism of nerve or heart-muscle cells, on how well the drug reaches different organs, how it is broken down in the liver or excreted by the kidney. Doctors can also predict with greater certainty how well a drug will be tolerated, having gained their experience from human cells and not animals.

Therapy aside, genetic research is also expected to bring diagnostic improvements. This will help scientists better understand clinical processes such as Alzheimer's disease or ar-thritic conditions. Once the processes have been taken apart, ways can be found to treat the conditions. With the aid of genetic chips hardly bigger than a postage stamp, it will soon be comparatively easy to identify the individual variations in the genome of a healthy and a sick person.

One of the really ambitious targets of the "postgenomic era" is personalized medicine. Current practice is to try out which drug has the best effect on a certain heart patient. But instead, on the basis of personal genetic profiles drafted with genetic chips, it will be possible to determine in advance which form of treatment promises the patient the greatest relief with the least side effects.

But fully interpreting the personal book of life will probably remain wishful thinking on the part of scientists for a long time to come. Experiments on mice, in which specific genes were eliminated, have shown that it is often impossible to predict how healthy, or otherwise, the animal will be on the basis of individual genetic traits. This should be taken as a warning against inferring that a supposedly negative gene in humans automatically indicates a health defect. But genetic researchers remain confident that patients will soon benefit from detailed information on their individual genetic codes. In members of families with hereditary cancer of the colon, for instance, doctors can search for a genetic characteristic causing the disease. Patients with the defect would then be advised to have a prophylactic operation.

But another instance, the identification of a breast cancer gene in families exhibiting hereditary breast cancer, highlights the complicated issues arising from predictive genetic tests. There is not enough information to say for sure whether a woman possessing this gene will actually develop a cancer. Nor is it known whether the breast cancer will develop when the patient is 35 or not until she is 75. Since there is no certain way of preventing the outbreak of the disease, the only advice is to go for regular check-ups in young adulthood.

The decisions made necessary by genetic tests may be stressful, too. A person can be overwhelmed with anxiety when he or she is confronted with the prospect of a disease such as Chorea Huntington. Although CH ultimately leads to dementia, those affected are initially healthy. They would then have to live with the certainty of falling prey to the affliction in their middle age. To prevent discrimination against people in this situation, legislators must ensure that genetic information remains confidential.

Many people are also concerned over the question of how to act on the results of predictive tests on unborn babies. Diagnoses using genetic chips that scrutinize a host of genetic traits at once could soon become routine practice. But in man), cases proper interpretation of the results will not be possible for a long time. What is more, few people are presumably prepared to cope with the knowledge of their own genetic codes. For many diseases, it could take decades until the new diagnostic possibilities are followed by new therapies.

But Alzheimer's disease shows that genetic researchers are in a position to solve even the most intricate clinical processes. They have traced a whole number of genes that play a part in Alzheimer's dementia. In the process, they have come across a dysfunctional digestive enzyme in brain cells that is suddenly casting an entirely different light on the origins of the disease. So now they are setting their sights on the biocatalyst as the target structure, in the hope of soon finding a palliative.