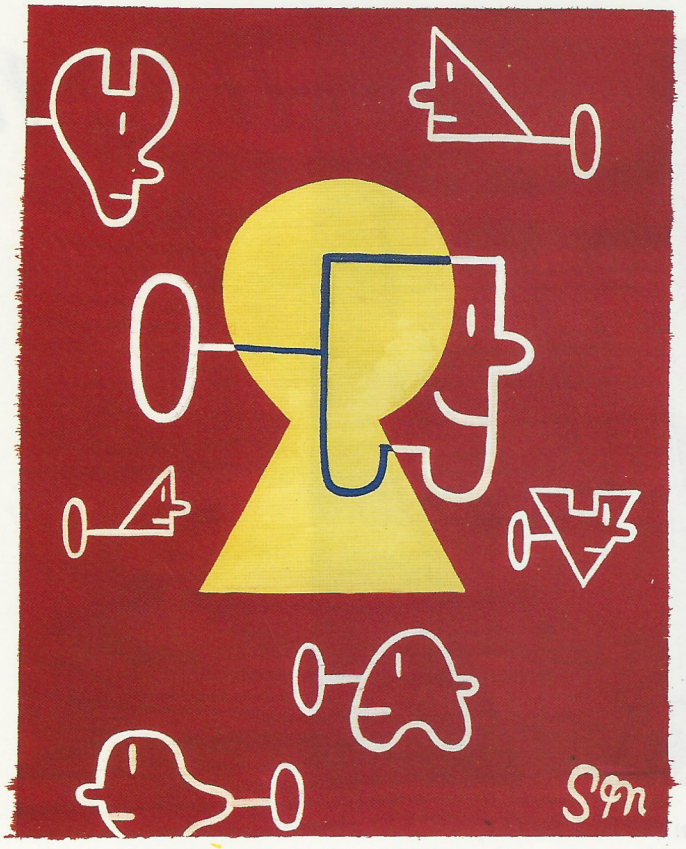
Molecular revolution

From contraceptive pills to antibiotics and pain relievers, drugs are one of the great success stories of Western medicine, but, unfortunately, to develop new ones is extremely costly and time-consuming. It can take decades to come up with a compound which will block pain or kill a virus. But now there is a new way of developing pharmaceutical compounds, which could not only lead to new drugs in a much shorter time, but also to much more powerful ones, drugs that traditional methods may never find. One company is already using this technique to look for drugs to combat HIV, the virus that causes AIDS.

The essence of this technique is a process called directed molecular evolution. The idea is that instead of a chemist trying to consciously design a compound to perform a specific task, he sits back and lets a group of molecules evolve themselves towards a solution. Having been inspired by the tremendous success of Darwinian evolution in nature, scientists have decided to use it themselves in their quest for the drugs of the twenty-first century.

Darwin's theory is alive and well in scientific circles. Now, "super" molecules are being bred in the quest for more effective pharmaceutical drugs. Margaret Wertheim reports



A leader in the field is Dr Gerald Joyce from the Scripps Research Institute in California. He explains that, in many ways, directed molecular evolution is similar to "the breeding programs practised by horticulturists and cat fanciers". "If one wants a redder rose or a fluffier Persian, one starts with those individuals that best exemplify the desired characteristic," he says. So, if you want to create a molecule that exhibits a particular chemical trait — for example, to prevent blood from clotting — then you can start with a number of molecules which show a small tendency to prevent blood clots, and then "breed" and evolve these until you get one which does the job very well. As with cats and roses, scientists are discovering that molecules, too, can be bred for specific characteristics.

The trick is to start with molecules that are capable of evolving. Nature has supplied us with two candidates: DNA and RNA. These have not traditionally been used as the basis for drugs, but scientists are finding that they can evolve to all sorts of useful medicinal properties.

To start off the process of molecular evolution, a scientist randomly generates literally trillions of different DNA molecules (this can be done automatically). All these are then let loose on the problem (for example, unclotted blood), and the scientist sits back and waits to see which ones do the desired task best. These achievers then become the parent stock for the next generation. They are subjected to random mutations (just as in nature) and their mutated offspring are in turn also thrown at the problem. With each generation, the objective is to get molecules which are increasingly better at doing the job.

The great thing about this technique, says Dr Joyce, is that "the molecules do all the work for us". What is more, the procedure can move at a rapid rate for, unlike cats and roses which can only produce a new generation once a year, there can be a new generation of molecules every day. Because of this speed, and because with each generation come trillions of variations, Dr Joyce notes that "it is a very powerful concept". By comparison, the traditional chemist who painstakingly works out his molecules one at a time "just doesn't cut it".

Directed molecular evolution is very new, but one company has already used it to produce an anti-coagulant drug which will help to prevent blood clots. It goes into clinical trials later this year. There are now more than a dozen new companies which have been set up to exploit the technique and, although many are highly secretive about what they are doing, one is known to be working on an anti-inflammatory drug, and another is working on a drug to inhibit the spread of HIV within the body.

Dr Joyce is not as interested in developing particular compounds as he is in understanding the mechanisms of molecular evolution itself. He is motivated, he says, by "a sense of respect and jealousy for nature". Given the extraordinary achievements using the processes of evolution, what might we be able to achieve if we applied these techniques to our own problems? ●

STEVEN MOORE