Can we eliminate the pests that ruin crops but leave their benign relatives unharmed? **Bijal Trivedi** explores a smart new strategy

It's a bug's death

THE environmental movement is often traced back to *Silent Spring*, the 1962 book in which Rachel Carson documented some of the harmful effects of pesticides on people and animals, and called for stricter controls. Half a century on, the book remains controversial but there is now no doubt that however useful pesticides are, they cause an immense amount of damage too.

Pesticide poisoning is a major health problem. Every year thousands of farm workers die of pesticide poisoning and millions more suffer severe effects, mainly in developing countries. A survey in Nicaragua last year concluded that 2 per cent of the country's adult population suffers pesticide poisoning annually. This kind of finding is not unusual.

Then there are the environmental effects. Many pesticides are toxic to a wide range of animals, and dose is often the only factor that restricts the killing to insects. They kill beneficial insects alongside harmful ones, which means that once farmers start using pesticides they often have to keep using them because there are fewer natural predators to help control pest populations. Some pesticides persist in the environment for decades and accumulate up the food chain. Plants genetically modified to produce biodegradable insecticides such as Bt are one way to solve these problems, but this approach does not work for all pests and there is intense opposition to GM crops in many countries.

Now, however, researchers are working on an entirely new generation of pesticides, one that promises to target individual species while leaving other animals unharmed. These could be sprayed onto plants like conventional pesticides or genetically engineered into crops. Already, one company is preparing for field tests of a spray targeting the Colorado potato beetle, a major pest (pictured, right).

The key to the new pesticides is gene silencing, and RNA interference (RNAi) in particular. In 1998, it was discovered that when a double strand of RNA (dsRNA) matching the sequence of a particular gene is injected into nematode worms, that gene gets switched off, or silenced.

RNAi may have evolved as a defence against viruses containing double-stranded RNA. Now, though, all plants and animals rely on RNA interference to help control the activity of their own genes. Remarkably, the effect can spread from cell to cell in some invertebrates: when dsRNA is injected into one part of the body, the matching gene often gets silenced in other parts of the body too. Just as surprising was the discovery that simply feeding dsRNA to worms could silence genes, although it was not as effective as injection. That result caught the attention of researchers like Steven Whyard, then working for Australia's national insect research institute, CSIRO Entomology, in Canberra. "We thought: it won't work in an insect, but let's give it a try anyway because if it does work we're off and running with something rather interesting," he says.

"Invasive pests are a serious problem – genetic tools that attack specific species would make for very powerful weapons"

It did work, Whyard and his colleagues at CSIRO patented the method, and by 2006 its pesticidal potential was becoming clear. A team led by Richard Newcomb at Plant and Food Research in Auckland, New Zealand, showed that gene activity in the guts and the antennae of the light brown apple moth, a major pest in Australia and New Zealand, could be greatly reduced by feeding them dsRNA.

A year later, two landmark papers published together in *Nature Biotechnology* proved that the effect was strong enough to protect plants from pests (vol 25, p 1231). One team, led by James Roberts of Monsanto in Chesterfield, Missouri, first fed a variety of dsRNAs to western corn rootworm larvae to see if any killed them. They found the most effective RNA targeted a gene coding for the enzyme v-ATPase. Next, the team genetically modified maize to produce this dsRNA in its roots. The modified plants suffered less root damage when infested with rootworm.

A second team, led by Xiao-Ya Chen, now head of the Shanghai Institutes for Biological Sciences at the Chinese Academy of Sciences, tried a less direct strategy. Cotton plants produce a natural pesticide called gossypol. Pests like the cotton bollworm, however, have evolved resistance, and Chen's team has found that this resistance depends on an enzyme called cytochrome P450. When bollworm larvae were fed plant material containing gossypol as well as dsRNA targeting the gene for cytochrome P450, the insects stopped growing and started dying.

These studies generated a lot of interest, but big questions remained. One is the effect of dsRNAs on humans (see "Is it safe?", page 36), and the other concerns specificity. If the dsRNA is designed to target a gene sequence that ›