# Hermes and the *housefly*

*Graeme O'Neill describes the recruitment of a traitorous gene to the struggle against agricultural pests and the vectors of human disease.*

In Homer's *Odyssey*, Hermes, son of Zeus, appears before Ulysses and his companions as a message-bearer from the Greek gods. In honour of this ancient tale, molecular biologists Dr Peter Atkinson of CSIRO's Division of Entomology, and Dr David O'Brochta of the University of Maryland have lent Hermes' name to an unusual gene with a similar role.

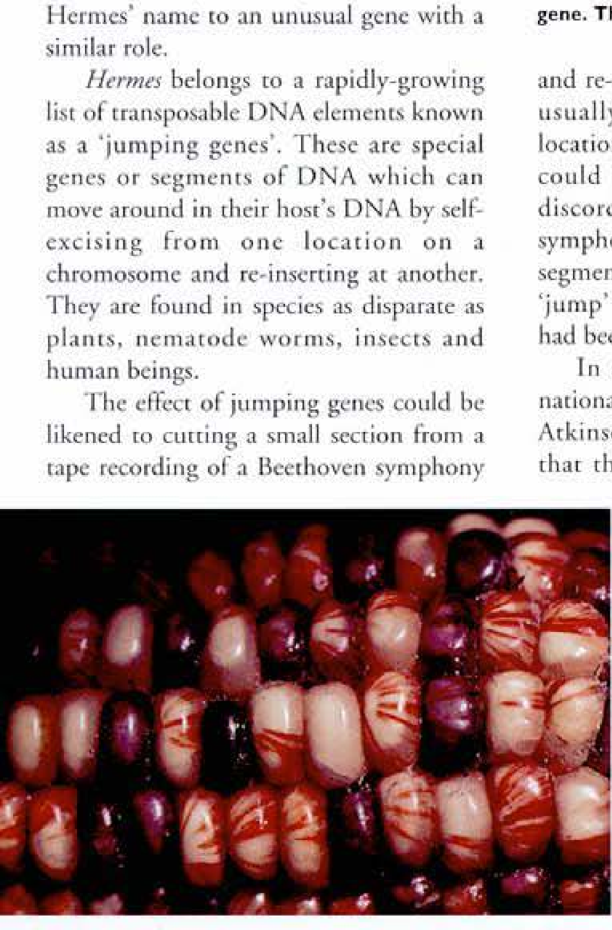
*Hermes* belongs to a rapidly-growing list of transposable DNA elements known as a 'jumping genes'. These are special genes or segments of DNA which can move around in their host's DNA by self-excising from one location on a chromosome and re-inserting at another. They are found in species as disparate as plants, nematode worms, insects and human beings.

The effect of jumping genes could be likened to cutting a small section from a tape recording of a Beethoven symphony


**The Hermes element inserts in the gene, disrupting its function. The plant geneticist notes the changed trait in the plant, then uses Hermes as a 'tag' to locate and clone the disrupted gene. The gene's function and location in the chromosome are then known.**

and re-splicing it into the tape elsewhere, usually with a disruptive effect. The location of the newly-inserted fragment could be identified by listening for a discordant phrase, a 'mutation' in the symphony. The original location of the segment could also be identified by the 'jump' in the symphony where the gap had been replaced.

In a paper published in the international journal *Genetics* last June (1996), Atkinson and O'Brochta demonstrated that the *Hermes* gene can be used as a genetic messenger to introduce novel traits into insect embryos. 'Harnessing the *Hermes* transposable element as a vector will permit the implementation of powerful genetic research programs to investigate the biology of insects significant to human health and welfare,' Atkinson says. For insect pests such as the Mediterranean fruit fly, the Australian sheep blowfly, or the malaria mosquito, *Hermes* may be the bearer of bad tidings, and an agent for sowing sterility in their midst.



**Mobile genetic elements with the ability to alter supposedly fixed hereditary traits were first discovered half a century ago in maize. The multi-hued kernels of Indian corn are examples of the elements' handiwork.**

## Familiar jumping genes

Half a century ago, with only classical breeding techniques at her disposal, American plant geneticist Dr Barbara McClintock proved the existence of mobile genetic elements that could alter or abolish supposedly fixed hereditary traits in maize. The multi-hued kernels of Indian corn are just one example of the handiwork of the two elements McClintock named 'Activator' *(Ac)* and 'Dissociator' *(Ds)*.

The Navajo Indians of North America used some of the more spectacularly patterned cobs of Indian corn as objects of reverence. Modern

Plants with variegated leaves, and rare, striped rose varieties such as *Rosa mundii* (top), and 'Harry Wheatcroft' (above) are familiar effects of jumping genes.

gardeners who prize plants with variegated leaves, and the novel 'sports' that have been found on popular plants such as roses and camellias, are also familiar with the effect of jumping genes. The famed cream, pink and yellow 'Peace' rose has produced at least half a dozen color-mutant sports, the most famous of which is the deep pink 'Chicago Peace'. Rare striped roses such as the mediaeval red-and-white striped *Rosa mundii*, and the modern red-and-yellow striped 'Harry Wheatcroft' are well known examples of jumping genes that modify genes for petal pigment. Vigorous climbing sports of other modern bush roses may also be the product of transposable DNA elements.

In 1983, the same year that Dr McClintock was awarded a Nobel Prize for her pioneering work, Dr Jim Peacock, Dr Liz Dennis, Dr Wayne Gerlach and Dr Bill Sutton from CSIRO's Division of Plant Industry used *Ds* as a genetic tag to locate and clone the world's first plant gene of known function: the alcohol dehydrogenase (*ADH*) gene of maize. From a mutant variety of maize lacking the enzyme, they isolated the gene and the *Ds* element that had disrupted it by 'jumping' into its DNA code.

McClintock's *Ac* and *Ds* elements, like many mobile elements, work in partnership. The 'master' element *Ac* encodes a transposase, a special DNA-cutting enzyme which excises the *Ds* 'slave' element from its original site on a chromosome and opens a gap elsewhere into which Ds inserts (see diagram below). Recombinant DNA technology has now shown *Ds* is essentially a degenerate version of *Ac*, lacking the sequence that codes for the transposase enzyme. Similar themes occur in other binary transposable-element systems.

Mobile DNA elements are ubiquitous in higher life forms. Their diversity suggests that some have been evolving for tens, even hundreds of millions of years as their original hosts founded new dynasties of species. Their DNA code provides clues to their origins. The *copia* elements of the common fruit fly *Drosophila melanogaster*, for example, show clear affinities with retroviruses, a specialised class of DNA parasites that replicate by inserting their genetic code into their host's DNA.

'Transposable elements can have adverse effects as they move around in the genomes of their hosts,' Atkinson says. 'They are the ultimate examples of selfish DNA.'

## An ointment in the fly

The *Hermes* story traces its beginnings to 1982 when molecular geneticists first used a P-element (another type of jumping gene) from *D. melanogaster*, to insert a new eye-color gene into fly embryos. They spliced the eye pigment gene into the middle of a P-element, then injected it into fly embryos.

Like many jumping genes, the P-element has two short, mirror-image sequences at either end, which are thought to facilitate a splicing reaction with the host's DNA; the host cell papers over the gaps with complementary DNA code. Should the mobile element jump out of the chromosome again, these fill-in sequences are able to repair the resulting gap, because their DNA code is complementary. They remain as a permanent footprint that betrays the transposable element's former presence.

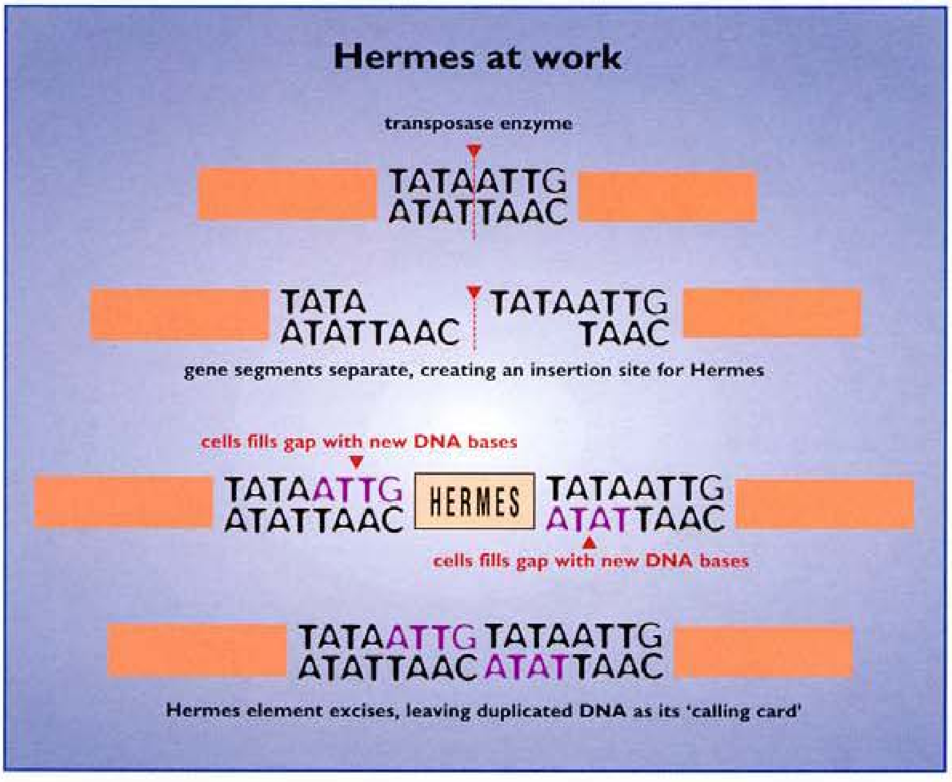
Insect geneticists' early hopes that the *Drosophila* P-element system would prove useful as a gene vector for a much wider range of insect species – or even mammals – came to naught. Like many transposable element systems in plants and animals, the P-element seems to be so closely adapted to its original host that it works only in *D. melanogaster* and a few closely related *Drosophila* species.

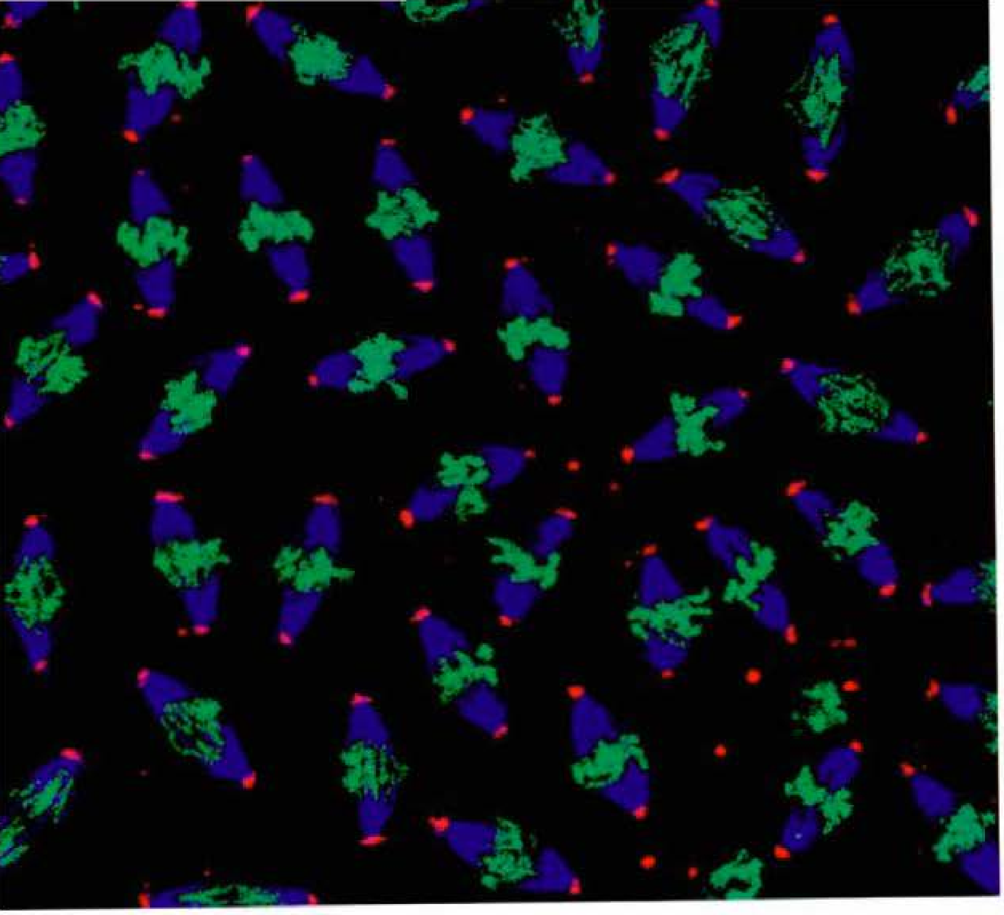
Transposase enzymes differ between species. While other fly species distantly related to *Drosophila* probably have their own variants of the P-transposase enzyme, they apparently cannot co-ordinate transposition when combined with alien P-elements.

But then O'Brochta and Atkinson's team found the element they named *Hermes*, in the common housefly *Musca domestica*. *Hermes* is a member of the *hAT* family of transposable elements, found in organisms as disparate as insects and plants. The hAT family includes McClintock's maize *Ac* element and the snapdragon element, *Tam3*, both of which transpose in distantly-related plant species including the tomato, tobacco, petunia and *Arabidopsis* from the cabbage family.

*Ac* and *Tam3* are now used to map genes in crop plants and to determine their function. For example, when introduced into a tomato embryo, *Ac* will often jump into an active gene, disrupting its activity and producing an observable change in the resulting seedling, such as a loss of resistance to a fungal disease. By locating the *Ac* 'tag', geneticists can recover the disrupted gene, so a previously anonymous gene can be linked to a specific trait in the plant.

Atkinson and O'Brochta expect that insect transposable elements with a wide





This image shows cell division in a fruit fly (*Drosophila*) embryo. The chromosomes are green, the spindle fibres blue and the centresomes red. The copia DNA elements of the common fruit fly show clear affinities with retroviruses, a specialised class of DNA parasites that replicate by inserting their genetic code into their host's DNA. (Image courtesy The University of Adelaide Confocul Microscope Facility: researcher, Ulrik John.)

host range will also become powerful tools for investigating insect genomes. The *hAT* family also includes the *Drosophila* element *Hobo*, which transposes successfully in the housefly, Queensland fruit fly *Bactrocera tryoni* and the cotton bollworm *Helicoverpa armigera*, the moth whose larva is the nemesis of the Australian cotton industry. *Helicoverpa* species are major pests of horticulture worldwide.

## A versatile performer

Based on their work so far, Atkinson and O'Brochta believe *Hermes* will prove capable of truly Olympian leaps. Its host range eventually may extend beyond insects to arthropods such as spiders, mites, millipedes and even crustaceans, groups that diverged from insects at least half a billion years ago.

The scientists say there are two possible explanations for the wide host range of *Hermes*. Genes required for the transposition of *hAT*-family elements present in other arthropod species may have so tightly conserved over millions of years that they can still activate introduced *Hermes* elements from *M. domestica*. Or, the *Hermes* element from *M. domestica* may not even require help from its new host; its own transposase may work perfectly in a wide range of species.

*Hermes*' ability to transform other arthropods appears likely to open up novel strategies for controlling agricultural pests, with or without pesticides, Atkinson and O'Brochta say. The principle was demonstrated in the 1980s when the Division of Entomology imported a naturally-occurring, pesticide-resistant predatory mite *Phytoseiulus persimilis* from California that controlled infestations of the two-spotted mite *Tetranychus urticae* in Australian apple and pear orchards.

Atkinson left CSIRO in early 1997 to join the University of California where is working on a number of insect species, including the Mediterranean fruit fly, *Ceratitis capitata*. The medfly is a major agricultural pest in California, Western Australia, Argentina and other parts of the world. A research group in Vienna is also working in this field.

*Hermes*' role in this control strategy will be to short-circuit the complex process of using non-transgenic techniques to breed sterile males. By swamping wild populations with sterile males, scientists have controlled the screw-worm fly in beef cattle herds, and reduced medfly infestations in Argentina. In these species, females mate only once, so if they mate with a sterile male, no progeny result.

'One immediate application for *Hermes* is in monitoring the success of sterile-male programs,' Atkinson says. 'You want a quick way of telling the sterile males apart from wild-type males, so you use *Hermes* to introduce an novel marker gene into sterile males.

'Potential applications also exist in medical entomology. Scientists in Colorado last year showed that it may be possible to make *Aedes egypti* mosquitoes refractory to the virus that causes dengue fever.'

Atkinson says these mosquitoes were not genetically engineered, because no vector system was available. Rather, the researchers infected the insects with a harmless engineered virus carrying an anti-sense gene to the dengue virus, with the result that the dengue virus could no longer replicate in the infected mosquitoes.

'It demonstrates a principle that has been driving research in this field for 14 years,' Atkinson says. 'If you can genetically-engineer mosquitoes so they can no longer transmit viruses or parasites, you may be able to reduce the incidence of diseases such as malaria, or sleeping sickness caused by Africa's tsetse fly.'

Other research groups have already shown that *Hermes* will transpose in *Aedes egypti*. This opens up the possibility of making *Anopheles* mosquitoes refractory to the *Plasmodium* parasites that cause malaria in human beings. Atkinson says that, using *Hermes* as a gene vector, it may be possible to disrupt a mosquito gene essential to the intimate relationship between the parasite and its insect host.

Atkinson and O'Brochta also hope aquaculture scientists will be able to use *Hermes* to map and study genes in crustaceans such as prawns, crabs and lobsters, and to introduce new genes conferring resistance to viruses and other pathogens that plague the industry.

### More about Hermes

O'Brochta D Warren WD Saville KJ and Atkinson PW (1996) Hermes, a functional non-Drosophilid gene vector from *Musca domestica*. *Genetics* Vol 142, March, pp 907-914.