# Flightless Aedes mosquitoes in dengue control

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## INTRODUCTION

Of the major vector-borne diseases (VBDs), dengue fever has re-emerged as a major public health challenge worldwide; with 2.5 billion people at risk of infection, more than 100 million cases and 25,000 deaths being reported annually. Even after more than 60 years of research, a licensed vaccine against the virus is still elusive,[1] and community-based vector control programmes have not been very successful either. Besides, as the Aedes mosquito is a day biter, individual protection using bednets is easier to preach than bringing into practice, thus accentuating the need for newer options in dengue control.

## THE NEED FOR INNOVATION

Focusing on manipulation of the Aedes vector that transmits the dengue virus could have long-term benefits. Sterile insect technique (SIT), initiated in the 1970s, which was based on the rearing and then release of sterile male mosquitoes, initially showed promising results, but had practical drawbacks. Overdose of radiation used for sterilisation of the insect affected the vigour of the sterilised males; bringing them is a disadvantage when compared to the native male mosquitoes in the competition for mating with females.[2] Besides the need for irradiation facilities to sterilise the mosquitoes, there are difficulties in transportation and problems in isolating only male mosquitoes for release.

## THE NOVEL TECHNIQUE

Release of insects carrying a dominant lethal (RIDL) technology, which involves introduction of a lethal or incapacitating trait in the female, has emerged as a powerful tool to overcome the pitfalls of SIT. Using a variant of this technology, a female-specific indirect flight muscle promoter from the *Aedes aegypti* Actin-4 (AeAct-4) gene has been used to modulate the transgenic strains of *A. aegypti*, thereby creating a repressible female-specific flightless phenotype using either two separate transgenes or a single transgene.[3] AeAct-4 is much more active in the pupal stage; more so in the female mosquitoes than in the males, predominantly in the indirect flight muscles.

Male Aedes mosquitoes have been modified to carry the promoter attached to AeAct-4. These genetically-altered males mate with females in the wild and pass on the gene to the females during the act of mating. When AeAct-4 is switched on in the flight muscles of the developing female of the next generation; it leads to death of the indirect flight muscle cells. As a result of non-development of these muscles, the resultant female progeny of the next generation are rendered flightless. The handicap of not being able to fly makes these females easy prey to their natural enemies, as well making it difficult to take a blood meal from the human host or find a mate. As AeAct-4 is not switched on in the flight muscles of the male, its flying ability remains unaffected by the modification.

## RESULTS

The flying ability of both male and female mosquitoes has been tested following the modification involving AeAct-4. This has been done by hatching the pupae in water-filled containers, and then observing the tendency of the newly hatched adults to fly away. The results have shown that 99–100% of the genetically engineered females were unable to fly while 97–98% of the genetically manipulated males could take off immediately on hatching out of the pupal stage.

## BENEFITS

As the mosquito reaches the adult stage before being physically affected by the modification, the modified larvae and pupae can still compete with their wild counterparts for survival, which is density dependent, thereby reducing the number of wild larvae and pupae who mature into adults. Besides, the need for irradiation, as is required in SIT, is done away with. The non-irradiated male is as healthy and efficient as wild males when competing for females. By the process of genetic sexing, the males and females can be easily separated before release, thus obviating the need for manual separation and its associated complications. The flightless female is, in effect, rendered sterile; as is unable to perform the wing oscillation song that is an obligatory requirement for courtship and mating.[4]

The genetically engineered eggs may be distributed rather than the release of the adults, thereby making the delivery cheap and less cumbersome as compared to SIT, where the

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dispersal ability of male mosquitoes is a major cause of concern. As the cryptic Aedes vector breeds in a variety of small containers, such as tyres, discarded tins, earthen pots, and water coolers, delivery of the modified vector in egg form is highly desirable.

As distribution of eggs requires no technical expertise, community participation may be ensured in a big way as a part of integrated vector-management programme. The technique is environment friendly and has no untoward health effects on the community when compared to the use of residual insecticides.

## LIMITATIONS

High cost of the technology is the main drawback, as the process of release of male mosquitoes is an expensive process. The technology is ideally suited to tackle the Aedes vector and diseases associated with it, as there are limited species of the "tiger mosquito". However, it will be difficult to apply the same approach for malaria control, since there are as many as 50 species of Anopheles implicating malaria transmission across the globe, and nine of them are involved in transmission of the disease in India alone.

In conclusion, although initial costs are prohibitive, the flightless female development approach holds promise not only for dengue control, but also for the potential control of other vector-borne diseases transmitted by Aedes, including chikungunya and yellow fever control. Further studies are required to explore the mate-seeking capability of the genetically manipulated male mosquitoes vis-à-vis their wild counterparts. The technology, being environment friendly, is a welcome tool in the fight against re-emerging vector-borne diseases, especially in developing countries which bear the brunt of these illnesses.

## CONFLICTS OF INTEREST

None.

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