GENEWATCH

THE GENETIC JUNGLE
By Guy Reeves

I have an image of walking through a tropical jungle sometime in the future. It looks and sounds just like an idealized jungle should: birds singing, luxuriously green, with the perceptible sound of insects doing the myriad of things that insects do. Yet despite the idyllic vista, I experience a sense of disquiet knowing how some of the organisms got into the picture. There are butterflies genetically modified to be resistant to a viral disease; an iconic orchid which was genetically modified to protect it from hybridizing its way out of existence with an accidentally introduced relative; and there are frogs with a genetically modified bacteria growing on their skins to help protect them from a fungal plague that had previously devastated their populations. The jungle certainly looks and feels more like a jungle in having its native butterflies, orchids and frogs. However, the presence of these GM organisms can also be seen as evidence of past failures to protect the environment, rather than as technological triumphs.

A case for genetically modified mosquitoes in saving endangered species

With the full knowledge that the above view of the future will in most people engender a fair degree of disquiet, including myself, I will nevertheless argue in favor of developing (though not necessarily using) an approach that could reasonably be seen as a first step down this road.

The Hawaiian Islands are the bird extinction capital of the world and approximately 70% of native Hawaiian bird species are already extinct or endangered. Bird malaria (avian malaria) is a significant factor in the continued loss of bird species. The mosquito that spreads avian malaria was accidently transported to the Hawaiian Islands in the 1820s, with the avian malaria parasite arriving about a hundred years later. Since then, many bird species have been in a race to evolve resistance to the disease. Some species have already won this evolutionary race with the malaria parasite and continue to thrive, while some have lost and gone extinct, while others teeter on the edge of extinction.

The last known Po'ouli individual died in 2004, its extinction was attributed to a combination of malaria, non-native predators and habitat loss.

Part of the reason why avian malaria in Hawaii cannot be controlled is because both of our most effective tools against insect-spread diseases cannot be used. The application of chemical insecticides in the forest is not only extremely difficult, but any killing of non-target insects has the potential to disrupt the ecosystem. Despite decades of sustained effort to develop a vaccine for human malaria, there has been little success and, as such, there is no reason to expect that a vaccine for bird malaria will become available. Given these realities, is it inevitable that bird extinctions will continue to the point that almost an entire level of the Hawaiian ecosystem is permanently lost?

What are genetically modified mosquitoes and how could they be useful?

A number of diverse genetic approaches to control insect-spread diseases are at various stages of development. For example, more than 13 million Aedes aegypti mosquitoes, which are genetically modified to be partially sterile, have already been released into the wild in Malaysia, Brazil and the Cayman Islands (releases have also recently been proposed in Key West, Florida). Another interesting approach is the development of a fungus which infects mosquitoes, that has been genetically modified to block malaria transmission.

However, the use of GM mosquitoes in Hawaiian bird conservation is based on a different approach, in which synthetic disease-resistant genes are introduced into populations of the mosquito species that spreads avian malaria. These genes would sustainably stay in the chromosomes of the wild mosquito population and stop them spreading malaria. The driving of genes into wild populations is not easy, but already two systems have been developed in the laboratory, and more are in development. Some systems allow these introduced genes to be completely removed from the wild if desired. This work is largely motivated by the goal of controlling human diseases spread by insects, like human malaria and lymphatic filariasis, and not by the conservation role discussed here. A synthetic gene that is substantially effective in preventing mosquitoes from transmitting avian malaria has already been developed.

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is ever to be used in conservation, it should at some point be possible to argue to local residents that the introduction of about 5,000 bases of foreign DNA into the 600,000,000 base genome of the Culex quinquefasciatus mosquito (every base of which is foreign to Hawaii) is a safe and attractive alternative to other available solutions.

Are there alternative solutions?

Avian malaria is only one factor in the continued loss of bird species and there are intensive (but rather under resourced) efforts to address the impact of habitat loss and non-native predators. However, efforts to develop ways to directly reduce the impact of malaria have made little progress. This is despite a range of realistic proposals, which include:

1. Eradicating the mosquito through the coordinated large-scale release of sterile males, which effectively prevent wild females from having any offspring (males never blood feed). This technique, first developed by American scientists in the 1950s, was used to eradicate screwworms (which were non-native flies) from most of continental USA, in an area more than 100 times the total size of the Hawaiian Islands.
2. Eliminating feral pigs from some reserve areas may create malaria free refuges for birds because the action of feral pigs feeding creates pools of water where mosquitoes breed.
3. Providing animals with small amounts of food that includes a drug that is harmless to birds and mammals but is lethal to mosquitoes when ingested during blood feeding could result in areas with fewer mosquitoes. A number of drugs routinely used for treating worm infections in people and animals have this property.

Surprisingly, none of these have been vigorously evaluated in the context of Hawaiian conservation, despite the fact that this could be achieved for much less than the cost of building one mile of freeway. In contrast, the development of GM mosquitoes has over the last decade attracted more than $30 million to address pressing human health problems like human malaria and dengue fever. The possibility that the resulting technological advances could also be harnessed to save species is an appealing one. However, if GM mosquitoes are ever used for conservation purposes, failure to vigorously pursue alternative approaches is likely to prove critical in retrospectively resolving the question posed at the start of this article. If simple and available solutions appear to have been ignored in favor of complex genetic techniques, the imagined 'genetic jungle' may in fact represent a realistic outcome.

***Guy Reeves**, PhD, is a researcher at the Max Planck Institute for Evolutionary Biology in Germany and is currently developing genetic systems that could drive disease resistance genes into insect populations in a reversible manner. However, he would be content if the application of alternative, more attractive approaches meant that these techniques were not used outside of the laboratory.*
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