

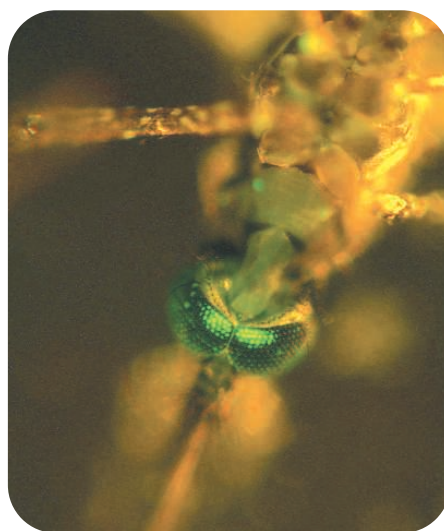
## GENETICS

## Selfish Genes Could Help Disease-Free Mosquitoes Spread

“Inspired by a true story”—that could have been the subtitle for a new study that brings the idea of disease-fighting mosquitoes a step closer. Researchers borrowed an idea from real life and, like Hollywood screenwriters, adapted it to suit a different plot.

The paper, published online by *Science* this week ([www.sciencemag.org/cgi/content/abstract/1138595](http://www.sciencemag.org/cgi/content/abstract/1138595)), addresses a crucial but often overlooked question: Even if you can make mosquitoes unable to transmit disease, how do you enable them to “replace,” or outcompete, the natural population? The study team, led by molecular biologist Bruce Hay and postdoc Chun-Hong Chen at the California Institute of Technology in Pasadena, answered it by producing a set of “selfish” genes in *Drosophila* fruit flies. The same principle could be applied in mosquitoes as well, they say. “This the most exciting thing I have seen [in this area] for a very long time,” says Jason Rasgon, an insect geneticist at Johns Hopkins University in Baltimore, Maryland.

The plan to battle disease using transgenic insects has been around for years. Scientists have already spliced into mosquitoes genes that



**Leg up.** A new study suggests a way to make transgenic insects—such as this malaria-resistant mosquito, created by a team at Johns Hopkins University—spread rapidly.

make them unable to transmit dengue, a painful viral disease, and the rodent form of malaria. A malaria-resistant version of *Anopheles gambiae*,

the mosquito whose bite kills more than 1 million people a year, is expected to arrive soon. Almost \$40 million from the Bill and Melinda Gates Foundation has given the field a big push and may help pay for trials in giant greenhouses within a few years.

Yet one big question remains: Nobody quite knows how to give an introduced resistance gene an evolutionary leg up so that it becomes widespread. Natural selection alone probably won't do it. It's true that having a virus or parasite reproducing in its body does reduce a mosquito's fitness, and a lab study published in the *Proceedings of the National Academy of Sciences (PNAS)* last week showed that malaria-resistant mosquitoes beat out their nonresistant rivals in the struggle for survival—if both were feeding on malaria-infected mice. In real life, however, only a small proportion of mosquito hosts are infected, says Rasgon, one of the *PNAS* paper's authors, so resistance doesn't offer a big enough benefit to make it race through a population. Some sort of active “driver” is needed.

Hay found inspiration for such a mechanism in a bizarre selfish genetic element first described in 1992 in a beetle called *Tribolium castaneum*. When female beetles carry even a single copy of this element, all their viable offspring have it, too; those that don't simply die. As a result, the element, called Medea, spreads through populations rapidly. ▶

## PROFESSIONAL SOCIETIES

## ACS Drops Iranian Members, Citing Embargo

The American Chemical Society (ACS) has reluctantly rescinded the membership of some 36 Iranian scientists after the society determined that having members in Iran violates U.S. law. The society hopes to reinstate them after obtaining a government license, a step that could set a precedent for other U.S. societies with Iranian members.

U.S. organizations are prohibited from doing business with individuals in Iran, Cuba, and North Korea, but an exemption permits the trade of informational materials. That provision allows U.S. scholarly societies, whose journals are a major benefit to its overseas members, to retain ties to members in those countries.

But ACS's stance changed after Assistant General Counsel David Smorodin reread the

embargo rules and concluded that selling publications to members at discount rates, a common practice, represents a service above and beyond the trade of informational materials. He also believes that membership benefits such as “insurance, career counseling, invitation to meetings, and educational opportunities” are not exempt under the rules, although he acknowledges that overseas members typically do not use those privileges. “We had no choice as a federally chartered organization but to comply with the law,” says Smorodin, adding that his interpretation of the regulations did not “win [me] any friends within the ACS.”

In January, ACS's membership office informed the society's 36 Iranian members that their memberships were being discontinued, although they could still purchase mate-

rials from the society at the full rate. The move angered David Rahni, an Iranian-American chemist at Pace University in Pleasantville, New York, and an ACS member, who says ACS should “refrain from allowing politics” to get in the way of scientific openness. Smorodin says the society will soon apply for a license from the Department of Commerce's Office of Foreign Assets Control allowing it to serve its Iranian members.

Other associations are troubled by ACS's proposed solution. “We have no plans to do anything similar,” says Judy Franz of the American Physical Society in College Park, Maryland, which also has members in Iran. “We would resist having to obtain a license to the extent we can.”

—YUDHIJIT BHATTACHARJEE

Researchers have proposed that *Medea* produces a toxin during egg development, just before meiosis. That way, even if female beetles have only one copy of the element, the toxin ends up in all of their egg cells. After fertilization, the toxin kills the zygote—unless it has inherited the *Medea* element from either its mother or father. In that case, *Medea* produces a special antidote just in time to neutralize the toxin.

All of this is just a hypothesis to explain *Medea*'s inheritance pattern, says Richard Beeman of Kansas State University in Manhattan, one of *Medea*'s discoverers, who is still trying to nail down the mechanism. But Hay and Chen decided they didn't need to wait for the answer to build the proposed system, toxin and antidote included, from scratch in fruit flies.

The team spent years engineering flies to

produce several kinds of toxins, such as ricin, in their egg cells, along with their respective antidotes. But making the insects produce exactly the right amount of toxin proved difficult. The team was luckier after it realized that the "toxin" didn't need to be a protein at all: It could also be the absence of one. They produced flies whose egg cells contain microRNAs that silence a gene called *Myd88*, whose protein product is crucial to pattern formation in the early embryo. Embryos resulting from these egg cells died. But if the embryos carried the team's *Medea* element, the "antidote"—in the form of an extra copy of the *Myd88* gene, switched on after fertilization—came to the rescue, and development was normal. "To create a synthetic *Medea*—what an amazing idea!" says Beeman.

And it worked. In cage experiments where

*Medea*-carrying flies were mated with wild-type counterparts, *Medea*-carrying flies took over in 10 generations or fewer. By stitching a resistance gene into the genetic element—right between the genes for the toxin and the antidote—it should be easy to make that spread through a population as well, Hay says, although that experiment still needs to be done.

Applying the same strategy in mosquitoes will be quite a bit of work, says Anthony James of the University of California, Irvine. Also, researchers have no idea whether the public will endorse the release of genetically engineered insects. But, says Kenneth Olson of North Carolina State University in Raleigh, the new study is a big step forward in making the notion of transgenic mosquitoes fly.

—MARTIN ENSERINK

## CLINICAL RESEARCH

# Testing a Novel Strategy Against Parkinson's Disease

One of the largest clinical trials ever for Parkinson's disease, announced last week by the National Institute of Neurological Disorders and Stroke (NINDS) in Bethesda, Maryland, is experimental in more ways than one, officials say. It will use a novel approach to test a nutritional supplement against a disease, with a goal of recruiting 1720 participants (half to receive a placebo). And the method of selecting the test agent, a supposed energy booster called creatine, was unorthodox as well.

In 2000, the institute began canvassing the community for compounds worth testing against Parkinson's disease and whittled a list of dozens down to a handful of candidates for so-called futility trials. Rather than show whether the compounds work, these small studies suggest whether a drug is futile in combating the disease.

Creatine is the only compound of four examined so far to pass. NINDS is beginning to recruit early-stage patients for a large, phase III trial to see whether a purified medicinal version can slow the disease's progress. In another twist, the institute may add more compounds to the trial if they pass futility studies. "The whole thing is unusual," agrees Debra Babcock of NINDS of the creatine trial, for which she

is the scientific director. "It's a very new clinical trial for us and a new approach for disease intervention."

Babcock declined to give precise numbers on how much the trial will cost. But the entire venture, including futility trials of other potential Parkinson's compounds, is now expected to cost about \$60 million, \$20 million above the initial estimate, Babcock says. These estimates are "fuzzy," she explained, because NINDS doesn't

more energy and protecting mitochondria, which in Parkinson's patients seem to malfunction, leading to cell death. Whether creatine is promising enough to justify a massive, long-term clinical trial in a time of tight budgets is up for debate. "To be honest, I think the evidence is not tremendously strong" that creatine can help, says J. Timothy Greenamyre, director of the Pittsburgh Institute for Neurodegenerative Diseases at the University of Pittsburgh in Pennsylvania.

Another question is whether enough patients will sign up, because volunteers risk receiving a placebo. Recruiting may be "a major logistical challenge," says Joel Perlmutter, a neurologist at Washington University School of Medicine in St. Louis, Missouri, whose center is one of the 51 participating. Babcock hopes the offer of pure creatine will attract volunteers.

Although Perlmutter considers creatine promising, he's uncertain about its mechanism and how it might work against Parkinson's disease. Still, "even if creatine completely bombs," says Perlmutter, the trial may still help teach researchers how to run large-scale Parkinson's trials and identify new biomarkers.

—JENNIFER COUZIN

With reporting by Eliot Marshall.



**Top candidate.** A medicinal version of creatine, a popular nutritional supplement, will be tested as an anti-Parkinson's agent.

know how many futility trials it will run or how the creatine trial will evolve in the 7 years it's expected to last.

Creatine, which is available over the counter in health food stores, is thought to help boost ATP levels in cells, giving them