Infecting Mosquitoes May Keep Them from Infecting Us

Life-shortening bacterium could beat mosquito-borne disease

By Bianca Nogrady

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Even in the teeming and varied world of bacteria, *Wolbachia* is something of a standout. Within its insect host, the bacterium acts as a gender-bending, egg-killing, DNA-hijacking parasite that is passed down from one generation to the next via the female to her eggs. Hosted by at least one fifth of all insect species, it is possibly the most prolific parasite on earth. But now Wolbachia itself is being hijacked, to help humans gain the upper hand in the long-running war against mosquito-borne diseases.

In particular, a team at the University of Queensland in Australia and Central China Normal University in Wuhan zeroed in on a *Wolbachia* strain that halves the life span of its natural, fruit-fly host. The scientists have successfully introduced it into an entirely new host: *Aedes aegypti*, the mosquito that spreads the virus that causes dengue fever, which produces severe, flulike symptoms and rash—and, in its more dangerous hemorrhagic form, can be fatal in about 5 percent of cases.

Wolbachia's life-shortening effect does not appear to inconvenience *A. aegypti*'s reproduction. In fact, it confers an advantage to infected females by killing the eggs of uninfected females fertilized by an infected male. But the bacterium could be disastrous for the dengue virus, which has a long incubation period: it takes up to two weeks to invade the mosquito, replicate, get into the mosquito's salivary glands and then spread to a new host, explains Scott O'Neill, an entomologist at the University of Queensland.

If infected with the life-shortening *Wolbachia* strain, the mosquito may not live long enough for its dengue passenger to incubate and move on. Given that newly hatched female mosquitoes usually wait two days before they have their first blood meal and potentially take the dengue virus onboard, the 21- to 27-day life span of a *Wolbachia*-harboring mosquito therefore offers only a narrow time frame for dengue to incubate and spread.

Researchers have also found another surprising side effect. Infected mosquitoes attempted to bite human volunteers more frequently but could not draw any blood. On closer inspection, the team discovered that the mosquitoes' proboscises had become "bendy" and could not penetrate the skin.

It was an unexpected windfall, O'Neill remarks, as a mosquito that cannot bite cannot transmit dengue—or any other disease. "We're talking about shortening life by 50 percent, but they're already dead if they can't stick their stylet into somebody's arm," he says.

The research has attracted considerable interest, particularly in far-north Queensland, which is in the grip of a major dengue outbreak. Current methods of dengue control focus on eliminating the mosquito's favorite breeding sites in containers of water, explains Scott Ritchie, a medical entomologist at Queensland Health, the state's health department, and the University of Queensland. But it is no easy task.

"It's very labor intensive, as guys have to go house to house and try to get rid of containers that are holding water, and in a lot of areas those containers are holding potable water that people need," Ritchie says. Although this tactic is reasonably successful in urban Australia, it would be far less practical, or safe, in the densely populated shantytowns of Brazil's Rio de Janeiro, for example. In which case, a biological control such as *Wolbachia* that spreads naturally starts to look pretty enticing.

Wolbachia appears even more attractive considering its potential application in controlling other insect-borne diseases, such as malaria and the tsetse fly's sleeping sickness. Filariasis might be an especially good target because the parasitic worms that cause the illness incubate "for a long period," says Ramakrishna U. Rao, a molecular parasitologist at the Washington University School of Medicine in St. Louis. Rao notes, however, that the success occurred in the laboratory, "so what happens if you actually introduce [*Wolbachia*-infected mosquitoes] into the field?"

O'Neill and his colleagues are setting up such field trials, bringing wild, uninfected mosquitoes into outdoor cages of infected individuals, to see if the *Wolbachia* strain will take over under natural conditions. (Thankfully this strain does not show the gender-altering effects of other *Wolbachia* varieties, such as the one that infects wood lice; otherwise it might reduce the fitness of the infected population.) Researchers hope the *Wolbachia*-harboring mosquitoes will gradually come to dominate—and along the way get rid of the mosquitoes' other, less human-friendly passengers.

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