Australia's mosquito men

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An international team of scientists led by Professor Scott O'Neill of Monash University has developed a natural method to reduce the spread of dengue fever across the tropics. He and fellow Australian, Professor Paul Young of the University of Queensland, are part of the global effort to beat and treat dengue, a disease which infects 390 million people every year.

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When Professor Scott O'Neill and his team tell people they are going to release hundreds of thousands of mosquitoes in their neighbourhood, like they have in five countries around the world, the initial response isn't always positive.

"It's a little bit of a challenge," O'Neill says. "The public health message for the last 50 years has been to kill mosquitoes, and then you have these scientists letting them go… We've had to spend a lot of time working with communities."

With the support of residents and governments, O'Neill's mosquitoes are now buzzing around cities in five countries - Australia, Brazil, Colombia, Indonesia and Vietnam - as part of the *Eliminate Dengue: Our Challenge program*.

Their approach is to tackle dengue fever at its source: to restrict the growth of the virus in the mosquito itself.

The mosquitoes in these countries have been injected with bacteria called *Wolbachia*, which exist naturally in

about 60 per cent of insect species. When introduced to the mosquito *Aedes aegypti*, this bacteria restricts the growth of the dengue virus, making it significantly less likely to be passed on to people.

The mosquitoes carrying *Wolbachia* breed with wild mosquitoes and, if all goes according to plan, within a few generations almost all the local mosquitoes have the bacteria.

This, the researchers hope, should help stop the spread of dengue.

“We’ve been getting very promising results both in the lab and the field,” says O’Neill, who as well as being program leader is Dean of Science at Australia’s Monash University and Professor in the School of Biological Sciences.

“We’re hoping over the next four or five years we can show a major impact and then we’d like to move towards global rollout.

“Over the next 15 to 20 years we’d like to be situated in most of the countries where dengue is a major problem, and having a large impact on the disease.”

The *Wolbachia* method, O’Neill says, has several advantages.

“We’ve got a natural approach that has been shown to be safe for people, animals and the environment. It’s affordable, which is especially an issue in developing countries where dengue is a problem and the countries can’t afford a traditional insecticide-based control program. And from what we’ve done so far it looks like it’s sustainable: we apply it once and it maintains itself.”

Dengue, ranked by the World Health Organisation (WHO) as the most important mosquito-borne viral disease in the world, is proving difficult to beat.

An estimated 2.5 billion people live in more than 100 endemic countries and areas where dengue can be transmitted. Global incidence has increased 30-fold in the past 50 years, says WHO, and now an estimated 390 million people a year are infected with dengue, with huge economic impacts for the countries worst affected.

Up to 500,000 cases a year develop into the severe form of the disease, dengue haemorrhagic fever, causing 25,000 deaths.

“At the moment there’s nothing working for dengue control and, as a result, the problem is getting worse and worse,” O’Neill says.

Born in Gosford, on the New South Wales Central Coast, O’Neill has been working on dengue since he took up an associate research scientist position at Yale University in the US in 1991.

“I’ve always wanted to do work that would have potential impact,” he says. “As I’ve got older this desire to have an impact has grown larger within me.”

O’Neill arrived at Yale via an agricultural science degree at the University of Sydney (where he developed an interest in insects) and a PhD at the University of Queensland, in which he focused on mosquitoes and *Wolbachia*.

After 10 years at Yale, O’Neill decided it was time to bring his family back to Australia.

“You come to that junction where you stay and become an immigrant or you go back,” he says. “I went back.”

O’Neill spent 10 years at the University of Queensland in a number of roles, including Deputy Executive Dean, Faculty of Biological and Chemical Sciences, before taking up the Dean of Science position at Monash in 2011. The author of more than 100 papers, he has received awards including the Centenary Medal and the Mackerras Medal and is a Fellow of the Australian Academy of Science.

O’Neill’s dengue research received an important boost in 2005 when the Bill & Melinda Gates Foundation provided funding. His project became known as *Eliminate Dengue* a year later. Other funders include the Tahija Foundation, Wellcome Trust, Gillespie Family Foundation and Australian, Queensland and Brazilian governments.

“Philanthropic support has been incredibly important for us,” O’Neill says.

Can dengue really be wiped out? “We often dream about that,” O’Neill says. “We brand ourselves *Eliminate Dengue* to remind ourselves what our goal is.

“It’s an aspirational goal. If we were able to have a significant reduction in dengue globally we’d be delighted with that outcome. I think ultimately it will require a combination of approaches working together, and we would hope this would be one of the major ones.”

Australia has a strong tradition in tropical medicine research and a number of “very good dengue people” doing important work, O’Neill says.

Among them is Paul Young, Professor of Virology and Head of the School of Chemistry and Molecular Biosciences at the University of Queensland.

Young’s research into dengue is threefold: developing a vaccine, delivering a therapeutic compound and improving diagnostics.

Dengue, Young says, is often referred to as one of the “neglected diseases”.

“The pharmaceutical industry hasn’t focused its efforts on some of these diseases because they’re predominantly diseases of the developing world and there isn’t a perceived large market,” Young says.

Rather than developing new compounds to tackle dengue, which would mean a wait of 15 or 20 years before testing is complete and they can go into clinical use, Young’s team has been looking into repurposing drugs that have already gone through clinical trials for the treatment of other medical conditions.

“The idea is to take those drugs and try them against a new target, in this case dengue,” Young says.

In its latest breakthrough, the team has discovered a link between how a viral protein induces an immune response in dengue, and the way a bacterial product induces a similar response in bacterial infections.

“The reason that’s important is that the pharmaceutical industry has been working on drug-based approaches to these bacterial infections for 20 to 30 years, so there are a lot of drugs already on pharmaceutical shelves that have gone through clinical trials,” Young says.

Those drugs weren’t successful against bacteria but may be against dengue. “We can foreshorten all those years of development and go straight into clinical testing fairly quickly,” Young says. “We’ll be able to go into clinical trials, we think, within a year or so.”

Young predicts that could lead to a dengue drug being available in as little as five years.

Like O'Neill, Young was overseas when he first started researching dengue. Born in Brisbane, he graduated from the University of Queensland before getting his PhD at the London School of Hygiene and Tropical Medicine.

"In the mid-'80s there was very little research on dengue yet it was a huge problem in the tropics," Young says. He secured World Health Organisation funding and his dengue research began.

Young was appointed to a lectureship at the University of London and spent 11 years in England before returning home in 1989 to continue his work in Australia as Senior Research Fellow at the Sir Albert Sakzewski Virus Research Centre in Brisbane. He moved to the University of Queensland in 1991.

Funded primarily by Australia's National Health and Medical Research Council, Young's research involves international collaborations with partners including the Oxford University Clinical Research Unit in Vietnam and the Novartis Institute for Tropical Disease in Singapore.

He has been president of the Australian Society for Microbiology and the Australasian Virology Society.

Again like O'Neill, Young was drawn back to Australia by the prospect of a better lifestyle for his family, including two young children. But what also drew him home was the quality of the Australian science and research community.

"Without a good research environment I wouldn't have come back," he says. "So I came over to have a look and was absolutely blown away by the change in the Australian science community, and that's just grown. The last two to three decades have been extraordinary in terms of growth.

"Government funding has really pushed medical research infrastructure to the point where it's highly attractive to overseas players. We need to maintain that."

Through his international collaborations, Young is also aware of how much respect Australian scientists get around the world.

"It's the instant recognition of quality," he says. "In the past not too many people overseas would have thought about Australia when they talked about top-quality research, but they do now. There is wide recognition of the quality work that goes on here."

- Eliminate Dengue