Tennessee, Knoxville, who co-organized an NSF workshop about plant transformation last November. "And I think there's enough interest now in trying to come up with ways to fix the problem for major crops."

OBSTINATE CROPS

Some plants, such as the diminutive thale cress (*Arabidopsis thaliana*), the 'lab rat' of plants, are easily transformed using a bacterium that can add genes to plant genomes. Researchers insert the genes they want to test into the bacterium (*Agrobacterium tumefaciens*), and then coax the microbe to infect the reproductive cells of the plant. When the plant then produces offspring, some of them express the new genes.

But this does not work for many crops, and use of *Agrobacterium* triggers extra scrutiny from government agencies such as the US Department of Agriculture because it is considered a plant pest. As an alternative, researchers can use 'gene guns' that fire DNA-coated gold beads into plant cells. Those cells are then bathed in growth hormones and coaxed to regenerate a full plant. Some plants, such as maize (corn), readily bend to this treatment. Others, such as wheat and sorghum, do not.

For recalcitrant crops, it can take months of painstaking cell-culture work — optimizing growth conditions and hormone concentrations — to regenerate the full plant. The conditions needed for success vary not only from crop to crop, but also between plants of the same species.

Plant-transformation experts are a rare breed, says Joyce van Eck, one such specialist at Cornell University in Ithaca, New York. "There's a lot of art in what we do," she said at the London workshop. "It's difficult to find people with that training."

Add to that a dearth of funding for new methods, and researchers are left having to rely on decades-old techniques.

A BETTER WAY

But that could change as the hunt for alternatives heats up. Stewart and his collaborators have developed a robot that performs an established technique called protoplast transformation faster and more accurately than is possible by hand. The method uses enzymes to digest the cell wall, making it easier for researchers to introduce new genes. The problem of regenerating the whole plant, however, remains. Researchers used a similar approach, without robots, to perform CRISPR–Cas9 gene editing in a variety of plants, including lettuce and rice.

The cell-culture steps are still difficult. Stewart says that one person in his lab laboured unsuccessfully for two years to transform a tall grass that he uses for biofuel research. But the declining cost of enzymes allows researchers to perform more experiments, and the robotics improve throughput. Stewart is so enamoured with his creation that he has composed a song for it. "It's our baby right now," he says.

Others, such as Fredy Altpeter of the University of Florida in Gainesville, are hunting for a suite of genes that, when switched on or off, would make plant cells more amenable to transformation and regeneration from culture. "I think it will lead to much broader application of this technology, and will enable people who are not experts in cell culture to make those improvements," he says.

But researchers can't afford to wait for those developments, says Oldroyd. His project, which aims to develop cereals that use nitrogen from the soil more efficiently, will plough through tests of hundreds of transgenes using the old, cumbersome methods. "We just have to be patient," he says. ■

INFECTIOUS DISEASE

Infected mosquitoes fight Zika

South America hosts largest trials yet of Wolbachia *–infected insects to combat viruses.*

BY EWEN CALLAWAY

Two South American metropolises are enlisting bacterium-infected mosquitoes to fight Zika. The effort is the world's biggest test yet of an unconventional but promising approach to quell mosquito-borne diseases.

Mosquitoes that carry *Wolbachia* bacteria — which hinder the insects' ability to transmit Zika, dengue and other viruses — will be widely released in Rio de Janeiro, Brazil, and Medellín, Colombia, over the next two years, scientists announced on 26 October. The deployments will reach around 2.5 million people in each city. "This really has the potential to be a game changer in terms of vector control — the biggest thing since DDT," says Philip McCall, a medical entomologist who studies mosquito control at the Liverpool School of Tropical Medicine, UK.

Small numbers of *Wolbachia*-infected mosquitoes have already been released in both Rio de Janeiro and Medellín. But large biomedical funders have now announced US$18 million to scale up the efforts. "We really want to deploy quite quickly in large sections of these cities," says Scott O'Neill, a microbiologist at Monash University in Melbourne, Australia, and head of the Eliminate Dengue Program, which is leading the mosquito releases. Footing the bill are the Bill & Melinda Gates Foundation in Seattle, Washington, the London-based Wellcome Trust and the US and UK governments. Brazil's government is chipping in with an extra $3.7 million, O'Neill says.

VIRUS BLOCKERS

Wolbachia pipientis plagues some 60% of insect species worldwide — but doesn't naturally infect *Aedes aegypti* mosquitoes, the species that transmits Zika, dengue and numerous other viruses. The bacteria can hinder their hosts' fertility and influence the sex of offspring. They can also block viruses from reproducing in infected fruit flies and mosquitoes, as O'Neill and his colleagues discovered in the late 1990s. The team later developed laboratory populations of infected *A. aegypti*.

ISTOCK/GETTY

***Aedes aegypti* mosquitoes spread Zika, dengue and other viruses.**

When tens of thousands of these mosquitoes were released near the small city of Cairns in northern Australia in 2011, the bacteria spread rapidly among local *A. aegypti* mosquitoes; 90% of mosquitoes in a targeted area were infected within weeks. Tests in Indonesia and Vietnam found similar success. It's not yet clear whether the strategy also reduces rates of dengue infections in humans, but O'Neill's team has begun a trial in Yogyakarta, Indonesia, to find out.

The Eliminate Dengue team started releasing *Wolbachia*-infected mosquitoes in two Rio de Janeiro neighbourhoods in 2014, and in a suburb of Medellín in 2015. The bacteria block the replication of Zika and chikungunya virus (which caused widespread outbreaks in Latin America and the Caribbean in 2013–14). O'Neill's team hopes that the scaled-up deployments can combat those diseases, as well as dengue, which infected ▶

an estimated 1.6 million people in Brazil last year. The researchers plan to release mosquitoes in waves, survey the insects for infection and track the incidence of disease in areas with and without infected mosquitoes.

Other scientists are also testing *Wolbachia* to control mosquitoes. In Singapore, officials plan to release male *A. aegypti* mosquitoes infected with a strain of *Wolbachia* that renders their offspring infertile. A US biotechnology company is seeking approval to use a similar approach to combat related Asian tiger mosquitoes (*Aedes albopictus*), which carry dengue and chikungunya. In Guangzhou, China, scientists are releasing *A. albopictus* mosquitoes infected with *Wolbachia* each week, in large-scale field trials. And researchers in French Polynesia are trying the same strategy on another species of tiger mosquito.

MORE EVIDENCE NEEDED

Wolbachia has an impressive ability to surge through wild mosquito populations, says McCall, but proving that this limits human infections will be critical before the approach can find widespread use. If *Wolbachia* is to make a dent in mosquito-borne diseases, the technique will also have to be cost-effective and long-lasting, he adds. "If it works, it will be truly remarkable, but it has to still be working in ten years."

Another hurdle facing the tests in Rio de Janeiro and Medellín is the size of the cities — especially Rio, with its densely populated and hard-to-access *favelas*, says McCall. But if *Wolbachia* can combat Zika, dengue and chikungunya in such environments, "there is a very strong case for doing it for a range of other large cities", says Mike Turner, acting director of science at the Wellcome Trust. Widespread deployment of *Wolbachia*-infected mosquitoes would probably also depend on endorsement from the World Health Organization, he adds.

Public support could make or break the *Wolbachia* approach, says O'Neill, whose team spent years engaging with communities in Australia before deploying mosquitoes there. *Wolbachia* is already widespread among insects and it cannot infect humans, he notes. In Australia, researchers recruited schoolchildren, whom they dubbed *Wolbachia* warriors, to rear the eggs at home, learn about their development and then release the mosquitoes.

In Colombia, the Eliminate Dengue team has worked with "Casa *Wolbachia*" families to help with the release of mosquitoes, and even written salsa songs about the bacteria, says co-principal investigator Jorge Osorio, a pathobiologist at the University of Wisconsin–Madison. "We have communities asking us to spread more mosquitoes," he says. ■

Q&A Joshua Gordon
Psychiatry needs more mathematics

The US National Institute of Mental Health (NIMH) has a new director. On 12 September, psychiatrist Joshua Gordon took the reins at the institute, which has a budget of US$1.5 billion. He previously researched how genes predispose people to psychiatric illnesses by acting on neural circuits, at Columbia University in New York City. His predecessor, Thomas Insel, left the NIMH to join Verily Life Sciences, a start-up owned by Google's parent company Alphabet, in 2015. Gordon says that his priorities at the NIMH will include "low-hanging clinical fruit, neural circuits and mathematics — lots of mathematics", and explains to Nature *what that means.*

NIH

What do you plan to achieve in your first year?

I won't be doing anything radical. I am just going to listen to and learn from all the stakeholders — the scientific community, the public, consumer advocacy groups and other government offices. But I can say two general things.

In the past 20 years, my two predecessors, Steve Hyman [now director of the Stanley Center for Psychiatric Research at the Broad Institute in Cambridge, Massachusetts] and Tom Insel, embedded into the NIMH the idea that psychiatric disorders are disorders of the brain, and to make progress in treating them we really have to understand the brain. I will absolutely continue this legacy. This does not mean we are ignoring the important roles of the environment and social interactions in mental health — we know they have a fundamental impact. But that impact is on the brain.

Second, I will be thinking about how NIMH research can be structured to give payouts in the short, medium and long terms.

How has neuroscience changed since you completed your medical residency in 2001?

The advent of incredibly powerful tools to observe and alter activity in a subset of neurons, such as optogenetics, has been transformational. It is allowing us to get at questions of how neural circuits produce behaviour — a research approach that may soon generate new treatments for psychiatric disorders.

Which of the recent NIMH programmes do you find particularly exciting?

One is the Human Connectome Project. The project has scanned the brains of more than 1,000 healthy people to generate individual maps of their neural circuitry, the 'wiring' in their brains that accounts for their particular personalities. At the NIMH, we have created standardized databases, designed by the scientific community, to store this information. The Human Connectome Project is going to be a tremendous resource for the field — maybe not quite as impactful as the Human Genome Project, but on that scale, I think.

A clinical programme that deserves as much attention, but perhaps doesn't get it, is the Coordinated Specialty Care project for individuals facing their first psychotic episode. Some small studies have shown that coordinating different clinical and social-support programmes helps individuals to cope better.

Is this an example of 'low-hanging fruit'?

Yes. We are now looking for similarly significant clinical problems where good, evidence-based interventions exist but are not widely adopted. For example, we have a range of screening tools that we think can help reduce the suicide rate, which has been rising in the United States. It could be advantageous to incorporate universal suicidality screening as a matter of routine into all emergency rooms.