CASE STUDY

JULY 2026

Resurrecting Plant Immunity With Large-Scale Protein Engineering

In just one year, Resurrect Bio is able to achieve what most breeders take ten years to do. They have built an efficient and rapid process for identifying key proteins involved in pathogen-driven suppression of plant immune systems, as well as engineering resistant variants. Twist fills a critical need in this process by providing rapid, accurate and reliable synthesis of gene variants on a large-scale. Ultimately, this work has the potential to improve global crop yield at a time when it's urgently needed.

Introduction

Resurrect Bio, a London-based biotechnology company, is on a mission to shift the tide of an agricultural arms race. Using a combination of their custom AI-prediction tool and a rapid in planta screening platform, the company is helping plants develop resistance to a wide range of pathogens, from oomycetes to fungi, bacteria, and insects.

Pathogens collectively reduce the global output of major crops by roughly 20% each year. With few other options, farmers have resorted to pesticide use to protect their plants. But increasingly strict regulations—motivated by the detrimental effect these chemicals have on the environment and human health—have put the agricultural industry under pressure to find new ways to combat pathogens.[1-3] Simultaneously, global food supplies are strained by the effects of climate change and a growing world population.[4]

"Our vision is to rapidly develop pathogen resistant plants that help the world increase its food production without increasing its pesticide use," explains Imogen Binnian, a Lead Scientist at Resurrect Bio.

To achieve this goal, Resurrect Bio has built an advanced trait discovery pipeline, one capable of rapidly honing plant immune receptors to resurrect pathogen resistance. Binnian says that "our platform allows us to do 10 years worth of trait engineering work in just 1."

To rapidly test candidate immune receptors, their pipeline requires the rapid, large-scale synthesis of both plant and pathogen proteins. "20,000 candidates is a lot of combinations to test in just a single experiment, let alone every month," Binnian emphasized. The team needed a reliable, accurate, and large-scale DNA synthesis provider. In Twist, they found the solution they needed.

"Twist helps us translate the benefits of AI into the wet lab," Binnian explains. "Their DNA synthesis is so accurate and cost efficient, we can now try many different variants, different mutation combinations, and target a wider number of residues. At this point, the vast majority of the genes we have in our freezers were made by Twist."

Fortified by AI and Twist's DNA synthesis, Resurrect Bio's pipeline may be the ally crops need in the fight against pathogens.

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>
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Evolving Plant Immunity

Plants have evolved complex immune systems to combat pathogens. This includes a diverse network of pathogen-detecting receptors.[5] A subset of these receptors bind to proteins released from invading pathogens, known as "effector" proteins. Recognition of effector proteins by immune receptors can trigger a signalling cascade that ultimately leads to the death of both plant cells and the pathogens they contain (**Figure 1**).

In response, pathogens may evolve a wide range of counter measures, one of which is an arsenal of suppressive effector proteins that dampen immune signaling, often by obstructing receptors or hindering downstream signaling partners.[6] In doing so, these proteins enable infections to take root. To survive, plants must eventually mutate immune receptors in such a way that maintains immune signaling while disrupting effector suppression. In this way, plants and their pathogens are locked in a molecular arms race.

For centuries, farmers have helped crops gain an edge by selectively breeding individuals for pathogen resistance. While once effective, Binnian and many others in the field believe a more pro-active approach is needed. "Traditional approaches take quite a bit of time and the results are difficult to control—you don't get to choose which mutations you're selecting for. You may accidentally bring along undesirable mutations whose effects can take years to manifest."

Rather than wait for mutations to randomly develop in the wild, scientists can use the tools of molecular biology—such as synthetic DNA, AI, and CRISPR—to precisely engineer plant genomes and bring about a desired phenotype.

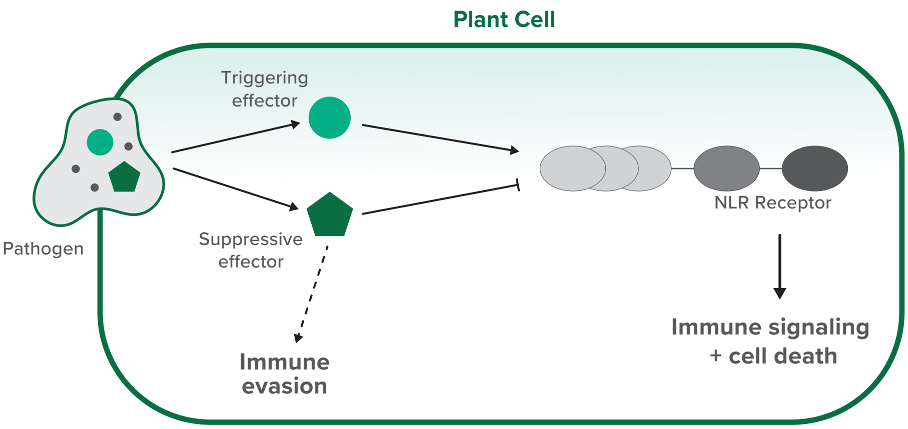

Figure 1. NLR-driven Plant Cell Immunity. Effector proteins are released from bacterial, viral, fungi, and other pathogens. These proteins can trigger nucleotide-binding domain and leucine-rich repeat (NLR) receptors, leading to immune signaling and cell death. Other effectors released by the pathogen can suppress NLR signaling, leading to immune evasion and durable infection.[5,7,8]

The Challenge: A Wet Lab Bottleneck

Resurrect Bio amassed a multimodal protein dataset to train FloraFold® on plant-pathogen interactions. With FloraFold®, the team can hone pathogen resistance using a three-phased approach (**Figure 2**).

“FloraFold® allows us to analyze both the plant and pathogen genomes, and then predict potential effector-receptor interactions in silico,” says Binnian. This greatly reduces the number of potential combinations that need to be investigated, but it can still produce tens-of-thousands of candidates, each of which will need to be validated in the wet-lab through a rapid in planta screening assay.

Synthesizing these receptors and effector proteins is a challenge in and of itself. But for the Resurrect Bio team, it is only half of the challenge. After candidate receptor-effector combinations are identified, the next phase involves mutating receptors in search of effector-resistant variants. Here again, FloraFold® is essential.

According to Binnian, “we can use FloraFold® to guide intelligent mutagenesis, greatly reducing the number of combinations we have to test in the lab. It’s way more efficient and allows us to cover more diverse mutation types than if we were going in blind and using random PCR for mutagenesis, as would have been done just a few years ago.”

Even with AI guiding them, the team must still synthesize and screen tens to hundreds of receptor variants in the lab. In both phases, effectively testing AI-identified candidates becomes the rate-limiting bottleneck.

“We have a big amount of synthesis to do in these projects, and it must be done both quickly and accurately,” says Binnian.

FROM ALPHAFOLD TO FLORAFOLD®

One of the challenges to leveraging AI against plant pathogens is the general lack of relevant training data.

“Because the immune receptors we’re interested in have human homologues, we can use public tools to effectively model these,” says Binnian. “But the datasets that feed tools like Alphafold have really poor representation of fungi, and none for oomycetes (a fungus-like eukaryotic organism).[7]”

This distinct vertebrate bias in proteomic and genomic datasets make it challenging to effectively leverage AI against pathogens like fungi and oomycetes. To overcome this challenge, the Resurrect Bio team built FloraFold®, a protein folding AI tool that’s specifically trained for plant and pathogen biology.

As Binnian explains it, “we’re collecting as much data as possible, both public and private, to correct for inherent biases in most datasets. We can do some of that with data from sequence and structure databases. But we’re collecting multiple layers of data, too, including wet lab validation studies we’ve done to record real protein-protein interactions—this allows FloraFold® to start looking for relevant and previously overlooked interaction domains.”

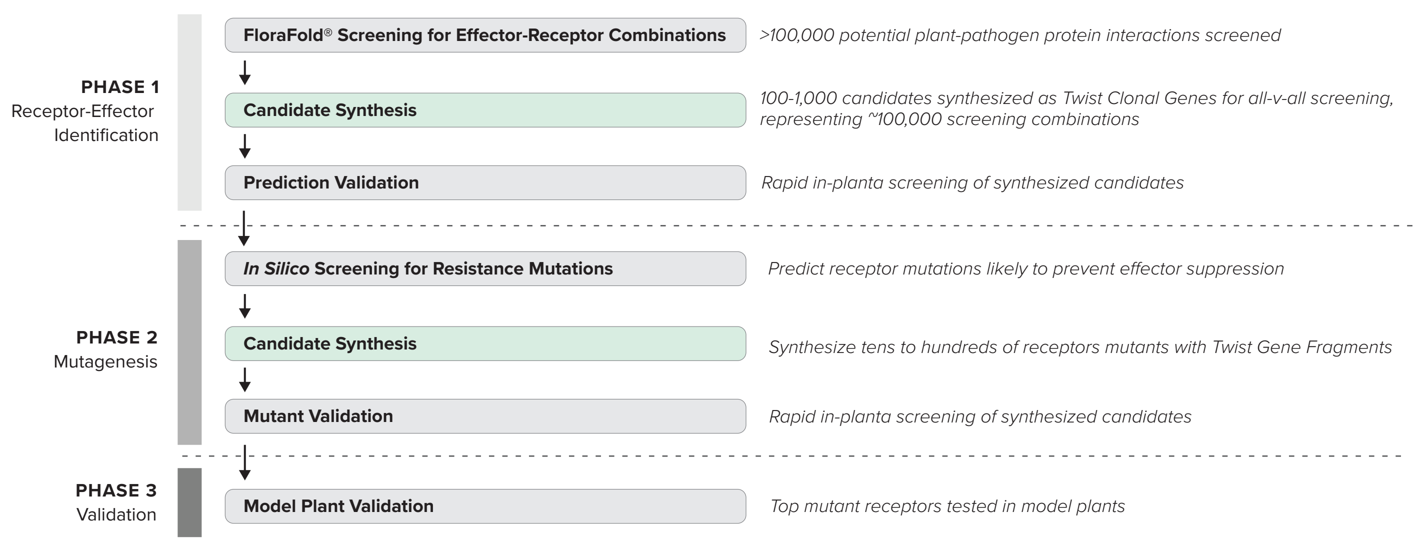

Figure 2. Resurrect Bio’s trait discovery Workflow.

The Solution: Twist Custom Genes

Resurrect Bio needed a way to synthesize many thousands of custom-designed genes. For this, they turned to Twist Bioscience.

In the initial phase of each project (**Figure 2**), plant receptor and pathogen effector proteins are synthesized as Twist Clonal Genes—0.3 – 7 kb genes that are cloned into the team's optimized plasmid construct. Twist clonal genes can be delivered within 10 business days, or, in the case of express genes, within 4 – 7 days*.

For receptor mutagenesis, the team chose Twist Gene Fragments. Gene fragments are custom designed, double stranded DNA fragments synthesized up to 5 kb in length. As one of the industry's leading platforms, Twist is able to synthesize gene fragments with high precision and high uniformity—meaning researchers like Binnian can trust that the variants they design are the variants they get.

As she explained, "one of the big reasons we went with Twist is the accuracy and scale of the DNA synthesis. We've established that even a single amino acid change—which can result from just a single nucleotide variant—can significantly affect receptor-effector interactions. But if synthesis errors cause mutations where you don't expect them, it could alter the protein's behavior in unpredictable ways and ruin the foundation of the screen."

There are quality checks, such as whole plasmid sequencing, that teams can use to ensure gene stocks are accurate. However, doing so is often not feasible. "It can cost £10 per plasmid," Binnian emphasized. "You should be able to trust what they send you is what they have said it is."

The speed of DNA synthesis turnaround time was also important to the Resurrect team. According to Binnian, "if we're doing a year-long project, we usually have only a month to synthesize and clone everything in order to meet the timeline, so synthesis has to be quick. This is something that Twist definitely does better than the competitors that we've tried."

Collectively, these features led the team to choose Twist. "We've just developed a really nice relationship with the Twist team," says Binnian. "They communicate very well and the speed of their synthesis is genuinely much better than what we've experienced with other companies."

With their advanced engineering pipeline, the Resurrect Bio team has already begun to produce encouraging results. "We're getting hits," Binnian emphasizes. "Now the bottleneck is data analysis."

In looking to the future, the team is hopeful. "We recently closed an $10.3 million series A funding round, which we will use to massively scale our platforms: We're aiming to increase our throughput by about 50x on the wet-lab screening, and that's motivated in large part by the good results we've already seen with Twist's synthesis capabilities—we know this system works and we know it can scale."

The team hopes to see some of the promising variants they've discovered enter field trial stages soon. Pathogens will remain a significant challenge for farmers the world over. But as they face increasing pressure to reduce pesticide use while also increasing their output, companies like Resurrect Bio offer a uniquely promising solution. ■

This timeframe refers to the typical processing and handling time within our facilities before your order is handed over the shipping carrier.

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Learn how Twist's DNA synthesis platform can support your protein engineering projects here.