

## Biomanufacturing Platform Generates Plant-Based Products — Including Biopesticides

Plants produce a variety of rare, specialized metabolites with unique properties that make them ideal for use as flavors, fragrances, food ingredients, pharmaceuticals, and agricultural chemicals. Despite this potential, however, the practical use of these compounds in commercial applications is often hampered by their low abundance in nature, which makes agricultural extraction a land- and resource-intensive process.

Manus Bio, a biotechnology company spun out of the Massachusetts Institute of Technology (MIT), is addressing these challenges by producing the same plant natural compounds through microbial fermentation. “We study the biosynthetic machinery of plants and then find ways to create sustainable manufacturing processes for these compounds that are up to tenfold cheaper,” says cofounder and CEO, Ajikumar Parayil.

To accomplish this, Manus Bio first uses the latest genomics, transcriptomics, metabolomics, and proteomics tools to elucidate the native plant biosynthetic enzymes needed to reconstitute a biochemical pathway to a desired ingredient. The company then applies its BioAssemblyLine bio-manufacturing platform, comprising technologies from metabolic engineer-

ing, protein engineering, and systems biology, to quickly engineer robust commercial strains.

Key to the company’s success has been a proprietary collection of universal chassis strains optimized for high yields of the main precursors of a variety of natural products. Modifying the high-performing chassis strains with advanced engineering tools allows the company to quickly and efficiently generate custom microbes, which are then cultivated in large-scale fermentation tanks to produce a variety of ingredients.

Although hundreds of thousands of compounds can be accessed through Manus Bio’s platform, one has received national attention for its potential to curb the rapid spread of vector-borne diseases. The Centers for Disease Control and Prevention (CDC) and U.S. Dept. of Agriculture have recently demonstrated that a rare but important component of grapefruit oil called nootkatone has potent repellent and pesticidal activity against many tick species, including the one that carries Lyme disease.

Lyme disease is one of the three most commonly reported infectious diseases in the U.S., with an estimated 240,000–440,000 new cases every year. Researchers and organizations

have struggled to address the growing tick population while minimizing the negative environmental and health impacts typically associated with the use of synthetic pesticides.

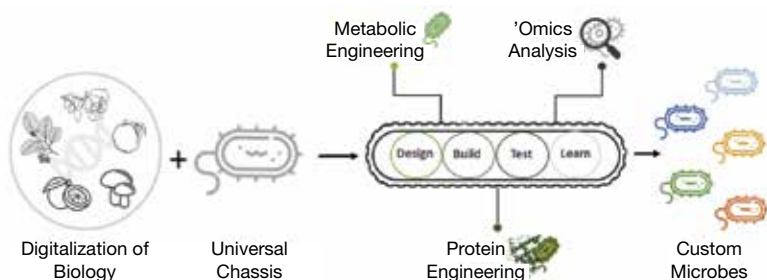
“Unlike synthetics, nootkatone is completely safe for aquatic life and bees and has no unintended effects on the environment,” says Christine Santos, CTO of Manus Bio. “Nootkatone’s long history of safe human consumption coupled with its potent acaricidal activity makes it an ideal ingredient to deploy in yard sprays and personal care products such as repellents. Using Manus Bio’s platform, we can bring the cost of nootkatone down by one or two orders of magnitude to achieve the levels needed for formulation into these products.”

With funding from the National Science Foundation (NSF), Manus Bio has already made significant progress toward this goal. The company has successfully developed a unique single-step microbial fermentation process for producing nootkatone. Manus Bio piloted the production process in its manufacturing facility in Augusta, GA, which has the capacity to produce hundreds to thousands of metric tons of product per year.

Manus Bio’s efforts have attracted the attention of Lyme disease organizations. Late last year, the company announced a partnership with the Global Lyme Alliance (GLA) to accelerate the development of nootkatone-based acaricidal products. “We are very excited to work with the GLA on bringing these products to market and, ultimately, make a significant positive impact on human health,” says Parayil.



This technology was funded through the NSF Small Business Innovation Research Program.



▲ The BioAssemblyLine platform recreates natural plant biochemistry in microbes. Manus Bio leverages tools in metabolic engineering, protein engineering, and systems biology to discover biosynthetic pathways and engineer commercial strains that can produce a variety of ingredients.

This article was prepared by the National Science Foundation in partnership with CEP.