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Cracking the code : Rick Melnick, Managing Partner & COO for DunhamTrimmer

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How manufacturing breakthroughs by three innovative companies changed the biologicals market â?? and changed whatâ??s possible for farmers

For decades, the use of biologicals in commercial agriculture has been a story of tremendous promise, and oftentimes, equally tremendous frustration. The microorganisms are remarkable. The modes of action are elegant. The science is rife with possibilities. Yet, for all of that potentiality, biologicals have remained in the margins of modern production agriculture, often viewed as too unstable, too inconsistent, or too difficult to manufacture at scale.

Now, that is changing. Not because the underlying biology has suddenly gotten better, but because three innovative companies have each independently solved a manufacturing problem that once seemed insurmountable. NewLeaf Symbiotics, CXC-AG, and GreenLight Biosciences work with entirely different biological platforms and achieved their respective breakthroughs through equally distinct scientific journeys. But their stories share an undeniable common thread: each succeeded by understanding biology deeply enough to stop fighting against it — and start working with it.

Together, these companies are helping to reshape what the biologicals industry can offer farmers while accelerating one of the most consequential shifts in modern production agriculture.

NewLeaf Symbiotics: Teaching a Microbe to Run a Marathon

Of all the age-old challenges in biological manufacturing, few are more stubborn than the problem of live gram-negative bacteria. Unlike well established gram-positive microbes such as *Bacillus thuringiensis* spp. *kurstaki*, which form naturally durable spores that can withstand spray-drying, storage, and handling with relative ease, non-spore-forming gram-negative microorganisms are notoriously fragile. Getting them from the fermentation tank to the farmer’s field in a living, active state has historically been so difficult that most of the industry simply avoided them altogether.

Enter NewLeaf Symbiotics, the St. Louis-based biologicals company that built its entire business around one such group: pink-pigmented facultative methylotrophs (PPFMs). These microorganisms are metabolically versatile, physiologically interesting, and (as NewLeaf has demonstrated) are capable of driving meaningful outcomes across biostimulant, biocontrol, and nitrogen-use efficiency applications. The challenge has always been making these microbes an accessible technology farmers can easily use.

“A grower wants to be able to use something just as easily as they do all the chemistries that are currently in the shed and on the shelf that they’ve been using for decades,” says Michael Frodyma, NewLeaf’s head of manufacturing and product development. “They want products where the application compatibility, the shelf stability, all those things are exactly like what they’re accustomed to using.”

While that sounds like a straightforward aspiration, achieving it with live gram-negative microorganisms is anything but. Frodyma says NewLeaf’s breakthrough came from a counterintuitive insight: the key to a stable end product was not going to be found in the downstream formulation steps — the drying, the excipients, the packaging — but in what happened to the cells before any of that began.

Frodyma describes the concept using a simple analogy. A person who is sick and exhausted cannot run a marathon, at least not very well. But that same person — if they have trained hard, rested well, and prepared properly — absolutely can. The organism is identical in both cases. What differs is physiological readiness. NewLeaf spent years learning exactly how to create “marathon-ready” cells: manipulating what the microbe receives during fermentation, when it receives it, and adapting the range of other fermentation variables that determine whether the living cell can survive spray drying, endure two years of shelf storage, survive tank mixing, and then perform in the field.

NewLeaf says the results speak for themselves. The company now reports two-year ambient shelf stability across its entire technology portfolio — a remarkable achievement for live, non-spore-forming gram-negative organisms. With its practical experience and advanced analytical tools, Frodyma says the company has moved from a roughly 50 per cent manufacturing success rate from its early production days to close to 98 per cent success at commercial scale. That is the kind of manufacturing reliability that is a prerequisite for mainstream agricultural adoption.

Given its success and the company’s intent focus on a defined class of organisms, NewLeaf believes it has also built a powerful pipeline advantage. When a new strain is identified from the company’s collection of nearly 13,000 unique isolates, the team has shown it can typically develop a commercially scalable manufacturing process in three to six months. That speed is only possible because NewLeaf’s underlying process knowledge in transferable across strains. It is a direct dividend of the company’s disciplined focus on PPFMs.

These advancements offer NewLeaf a broad range of exciting possibilities. The company launched its first bioinsecticide (TS201) in March 2024 and first biofungicide (TS601) in February 2026. By positioning these technologies alongside their existing biostimulants, NewLeaf has enabled the stacking of crop-specific biostimulant, bioinsecticide, and biofungicide solutions into a coordinated biological program, a program that growers can apply with the same ease and compatibility they expect from conventional chemistry. Mission accomplished.

CXC-AG: Intercepting a Conversation

The story of CXC-AG begins not in a boardroom or a startup incubator, but in the chilly soybean fields of southwestern Quebec in the mid-1980s. Dr. Don Smith had recently arrived at McGill University as an Assistant Professor when researchers there introduced the first soybean varieties capable of maturing in Canada’s short growing season. Smith watched those young plants emerge from the ground looking healthy, then fade to an unsettling pale yellow before finally, mysteriously, greening back up.

Cold soils were the culprit, he suspected. Optimal soil temperature for soybean nodulation (25° - 35° C) had been known for nearly a century, and Quebec’s spring planting soils were barely above 10. What Smith would discover was that the cold was disrupting the crucial first 12 hours of chemical signaling between soybean roots and their specialized symbiotic partners *Bradyrhizobium japonicum*, the nitrogen-fixing bacteria that form nodules on soybean roots.

That early signal exchange involves the plant releasing isoflavonoides such as genistein, and the bacteria responding by producing lipo-chitooligosaccharides, or LCOs — compounds that trigger the plant to accept the symbiosis. While this process had already been known to science, Smith was able to watch what happened when soil temperatures slowed the process enough to for him to clearly observe the interactions. He found that by preexposing the bacteria to genistein in the lab the night before they were applied in the field, the microbes generated LCOs in advance.

The finding was that treated plants didn't just nodulate faster. They came out of the ground faster, too. Soon, with two years of statistically significant data in hand from multiple field sites around Quebec, Smith was confident in the implications. LCOs weren't only signals for soybean nodulation they were helping the plants manage stress as well.

The discovery grew stranger and more interesting from there. A graduate student, at Smith's offhand suggestion, tested LCOs on corn — a crop with no connection to the soybean-*Bradyrhizobium* symbiosis whatsoever. "Neither of us expected it to work," Smith recalls, "but lo and behold, it worked on corn, too."

That moment brought forth an entirely new scientific understanding: LCOs were not merely nodulation signals. They were something older and broader — stress-response molecules that may have originated billions of years ago as signals between root-associated bacteria and plants. Four decades of research later, Smith's lab at McGill remains the only group in the world singularly focused on plant-microbe signaling at this depth.

LCOs work. That much is proven. LCO technology became the foundation of the Optimize (2003) and Jumpstart (2013) product lines that have since been sold commercially around the world. The problem CXC set out to solve was deeper than just proving efficacy. As François Lamoureux, CXC's President and CEO, puts it bluntly, "LCOs are notoriously hard to make. The challenge for CXC was figuring out how we can make LCOs more accessible to the farmer."

Lamoureux says the early manufacturing of LCOs was done using a pharma-style approach: porting the production mechanism into genetically modified *E. coli* bacteria to achieve meaningful yields. That route works, says Lamoureux, but it introduces a GMO organism into production, which carries its own regulatory and market-perception complications that CXC wanted to avoid, so they took a different approach.

Working alongside Smith and a team that includes several of his former students, now CXC's chief scientists, the company has developed methods to coax meaningful yields of high-purity LCOs from the original producing organism — *Bradyrhizobium japonicum* — without any genetic modification. Smith says the process exploits 40 years of accumulated knowledge about the organism's nutritional requirements, culturing conditions, and the subtle variables that most researchers would not think to manipulate.

The commercial stakes for this breakthrough are significant. LCOs function at extraordinarily low concentrations — on the order of 10 to the minus 11th molar, well within the range of the most sensitive hormonal signals in any biological system on Earth. The practical implication is that a single gram of properly produced LCO can treat an enormous number of acres, making cost-per-acre economics potentially transformational.

The Smith Lab and CXC have also identified a second molecule (product name Abio) — a bacteriocin-derived signal from *Bacillus thuringiensis* found inside the soybean nodule. Abio further boosts LCO efficacy when the two are combined, creating what CXC describes as a supercharged LCO platform.

Lamoureux says the Abio platform is at Technology Readiness Level (TRL) 9. Developed by NASA the TRL readiness scale was used to characterize the maturity of technologies during the acquisition phase of a program. TRL9 signifies a technology that is fully mature, fieldproven, and commercially operational in its final form. As such, CXC is in the process of identifying the right commercial partner with the scale and market access to bring its supercharged LCO (+Abio) platform technology to growers globally.

GreenLight Biosciences: An Answer from the Bottom of the Ocean

RNA interference (RNAi) — the mechanism by which double-stranded RNA molecules can silence specific genes in target organisms — has been one of the most exciting ideas in biological crop protection for more than two decades. The science, which won a Nobel Prize in 2006, offers something that conventional chemistry cannot: a mode of action so precisely targeted that a properly designed RNA molecule can silence a gene in a Colorado potato beetle without with an almost unprecedented level of specificity.

The obstacle for RNAi was never the science. It was the manufacturing economics.

Dr. Andrey Zarur, CEO of GreenLight Biosciences, describes the three historical routes to RNA production with the precision of someone who spent years eliminating each of them. Chemical synthesis — the approach used for therapeutic RNAs in treatments of some genetic disorders (such as amyloidosis), cardiovascular disease, and cancer — produces high-fidelity product but at costs ranging from tens of thousands to hundreds of thousands of dollars per gram. The process of enzymatic polymerization utilizes purchased nucleotide triphosphates as catalysts to synthesize RNA polymers in vitro, the method behind mRNA COVID vaccines. This method brings manufacturing costs down to thousands of dollars per gram, still a long way from viability for agricultural applications, where effective use might require use rates of ten grams per hectare.

The third route — fermentation using engineered bacteria — attracted enormous investment from heavy-hitters like Monsanto, Bayer, Syngenta, and others during the 1990s and 2000s. These companies theorized that if you could engineer *E. coli* to produce foreign RNA in a high-density fermentation, the economics should be favorable. In practice, however, biology refused to cooperate.

Zarur says the problem is fundamental and evolutionary. Every living organism on Earth has developed systems to recognize and destroy foreign RNA — because foreign RNA is the signature of infection. In *E. coli*-based fermentation, as foreign RNA accumulates, the bacteria respond by dramatically upregulating the production of nucleases that degrade the RNA. The result is a broad distribution of molecular fragments in the broth, only 1-2 per cent of which is high purity product. When sprayed on crops, the mixture largely failed, and the major companies eventually walked away.

GreenLight's conclusion was at once simple, complicated and unambiguous. They needed to eliminate the living cell entirely from the manufacturing process. But this created what seemed like an impossible engineering problem. RNA synthesis requires energy, specifically ATP, the universal energy currency of life, to phosphorylate the nucleotide building blocks needed for RNA polymerization. Organisms make ATP either through respiration, photosynthesis, glycolysis, or anaerobic metabolism. Once living cells were removed from the process, where would the ATP come from?

"The key to this whole problem became: can we supply energy to the system so that it can phosphorylate those nucleotides and drive this reaction forward?" Zarur says. "Simply elucidating that took a couple of years. But then figuring out how to make that energy took another eight years, because it had never been done before."

The breakthrough came from an unexpected source. In the alkaline volcanic vents at the bottom of the Atlantic Ocean — in a place called the Atlantis Massif — live organisms have thrived for 4.2 billion years with neither oxygen nor sunlight. These extremophiles produce ATP by extracting phosphate from inorganic molecules like calcium phosphate and iron phosphate in their surroundings, using a set of ancient enzymes that likely predate every other energy metabolism on Earth.

GreenLight surmised it could adapt those enzymes for industrial use. The original organisms worked in cold, high-pressure marine environments, drawing on insoluble phosphate sources that would simply precipitate out of a bioreactor. Researchers spent years engineering the system to function at room temperature, ambient pressure, with soluble phosphate sources, and at speeds sufficient for industrial production. When the first version of GreenLight's cell-free enzyme system worked, the resultant RNA cost about $100 per gram — 10 times cheaper than anything else available at the time. Within a year of hitting that milestone, however, iterative improvements drove the cost below $1 per gram, an astonishing reduction stemming from the high purity of the resulting product.

A mass spectrometry analysis of GreenLight's RNA shows essentially a single peak — approximately 99% of the product is the correct molecule at the correct molecular weight. That means that every molecule sprayed in the field is capable of affecting its target. That purity also proved critical for regulatory approval: GreenLight had to help the EPA develop an entirely new framework for evaluating RNA insecticides, including sequence analytics, bioinformatics demonstrating non-target organism safety, and environmental fate studies. That framework now exists and has been adopted by the Organisation for Economic Cooperation and Development (OECD).

Today, GreenLight has two commercial RNA biopesticide products on the market — Calantha, targeting the Colorado potato beetle, and Norroa — and is expanding rapidly. "We're sold out of everything," Zarur says. "We can't keep it on the shelves, and it's only May." Current production is running at approximately 5.5 metric tons of RNA per year, with the company aiming for 30 metric tons by year end — more RNA than was previously thought possible to manufacture. According to Zarur, the GreenLight pipeline is extensive.

Common Denominators

Three companies. Three entirely different biological platforms. Three very different manufacturing breakthroughs. And yet the underlying similarities are striking.

In each case, the biology was ready long before the manufacturing was. PPFMs have been known and studied for decades. LCOs were commercialized by a global agricultural company. RNA interference won a Nobel Prize. The science was not the bottleneck. Manufacturability was. Initially, NewLeaf could not stabilize living gram-negative cells. At the outset, CXC could not produce LCOs from non-GMO organisms at commercial purity and yield. In the beginning, GreenLight could not make RNA cheaply enough for field use. Biology becomes agriculture only when manufacturing catches up.

In each case, the companies' respective solutions required working with biology rather than against it. NewLeaf didn't depend upon formulation gymnastics to protect cells that weren't ready; it learned how to make cells that were ready before processing began. CXC didn't try to force a faster GMO production route; it leaned into 40 years of knowledge about the

original organism's biology. GreenLight didn't try to suppress the *E. coli* nuclease response; it removed the living cell from the process entirely and rebuilt biological energy chemistry from its most ancient roots. Likewise, across all three innovations, purity and consistency emerge as strategic advantages rather than technical footnotes. These innovations are not rooted in brute-force engineering solutions. They are solutions that stem from deep biological understanding.

The long-term implications of these manufacturing breakthroughs extend well beyond the individual products coming to market. They suggest a structural leap forward in how the biologicals industry will compete and how farmers eventually think about their input programs. If biological products can be manufactured with the stability, cost, purity, and performance consistency that conventional chemistry has long offered, they can officially transition from nice-to-haves to need-to-haves. And in a world of increasingly erratic growing conditions, tools that help crops perform under variable stress conditions are precisely what farmers need most.