**U.S. House of Representatives Committee on Science, Space and Technology**
**Subcommittee on Research and Technology**

# The Future of Biotechnology: Solutions for Energy, Agriculture, and Manufacturing


**Testimony of Dr. Martin Dickman**
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Thank you. Good morning Chairwoman Comstock, Ranking Member Lipinski, and members of the subcommittee; I appreciate the opportunity to testify here today and discuss emerging biotechnologies and applications in Agriculture.

My name is Marty Dickman. I am a University Distinguished Professor of Plant Pathology at Texas A&M University and the Christine Richardson Professor in Agriculture. I also serve as the Director of the Institute for Plant Genomics and Biotechnology (IPGB) in the Norman Borlaug Center at Texas A&M University. Dr. Borlaug and several colleagues were largely responsible in developing the "Green Revolution" of improving crops and importantly crop yields in the poorest of developing countries. Dr. Borlaug has been widely acclaimed for these efforts most notably through awards such as the Nobel Peace Prize, (the only agriculturist to be awarded this honor) U.S. Presidential Medal of Freedom and the U.S. Congressional Gold Medal. Dr. Borlaug's approach was straightforward but intense:  the use of scientifically rigorous breeding approaches to address and solve some of the most pressing food security issues of our time. He saved millions of lives; in fact he is known to have saved more lives than anyone in history.

We continue these efforts through the mission of the Borlaug Center which centers on a balance between fundamental and applied research. The mission of the IPGB is to develop plant biotechnology, genomics, and related life science technologies and to foster technology utilization and crop improvement through multidisciplinary research activities with model plant systems, field crops and horticultural plants. These are achieved by implementing modern and available technologies to increase our understanding of basic and applied (translational) issues in the Agricultural Biotechnology space, improve agronomic traits for crop plants and prepare young scientists with the necessary technical and conceptual tools to face the inevitable challenges that lie ahead.

As food safety and food security concerns continue and are likely to increase; it is clear a new Green Revolution is needed. The issues we face in developing such a new revolution now differ. There is increased urbanization which limits land availability, increased water use and energy demands, unpredictable climate changes coupled with pollution and soil erosion, and when taken together, collectively, all contribute to reduction in yield. We now face the task of growing more food on the same or even diminishing amounts of land.

In the remainder of my time, I will focus on three biotechnology approaches – (i) Synthetic Biology, (ii) the Phytobiome and (iii) Genome Editing -- and their impact with respect to agriculture and food production. I will highlight for illustration, some of the exciting work at our Institute [and other units] that are in progress to address these crucial food safety and food security concerns.

## I. SYNTHETIC BIOLOGY

The early 1970s ushered in a new paradigm for biological research--molecular biology. This change totally transformed the landscape of life science research, bringing with it a revolution in biotechnology. There is now a new paradigm, synthetic biology, which may be just as transformative for biological research as molecular biology. This is an exciting time for life science research.

Synthetic biology refers to the integration of molecular tools, engineering principles, and mathematical modeling to engineer organisms toward previously unattainable functions. This multidisciplinary discipline often requires integration of life sciences with engineering and modeling. Synthetic biology is still in its infancy of development, yet already has provided breakthroughs in crop production and in a wide array of other fields, including therapeutics, energy production and environmental remediation. Plants are being used to develop and commercialize novel and important products. For example, vaccines made against the anthrax toxin are being synthesized in plant "factories" grown hydroponically (which offers several advantages) using synthetic biology approaches to maximize production and purity. Similarly, plants are being used to synthesize artemisinin, an antibiotic/antimalarial toxin that is difficult to synthesize in sufficient quantity; again by application of synthetic biology. These approaches were built on several core research areas including genetic circuits design, metabolic engineering, high-throughput screening, and synthetic genome construction.

A synthetic biology design often depends on or integrates with the systems biology studies, and in some respects, synthetic biology is an extension of systems biology, which is the study of biological systems with the goal of moving beyond strictly observational studies to a new predictive view of biological systems. Systems biology is enabled by modern genomic tools, as well as computational resources, that allow high throughput analysis of the various components of the whole organism. During the past decade, synthetic and systems biology has delivered tremendous progress in crop improvement and other agricultural applications (see banana and cotton examples below) that are entirely dependent on biotechnological applications for success.

**Cotton/Gossypol**

Cottonseed has the potential to provide a protein to the world, especially for poor nations, but it contains gossypol, with major health issues such as male sterility and immune disorders. At Texas A&M, we were successful in developing a cotton plant where the seed did not contain gossypol but other issues of plant health arose. However, with the tools of synthetic biology and molecular biotechnology, we can address the plant health challenge and the outlook is a major inexpensive source of protein for the future population.

Cotton is a major crop grown in the state of Texas. It is well established that cotton seed is an excellent and abundant source of protein; nearly 25% of the seed dry weight. It is also known that gossypol, a common component of cotton seed and a plant defense compound has several characteristics making the seed unfit as food for human consumption or even as feed for non-ruminant animals for human consumption. Thus the application of cotton seed protein for food and feed is not viable. However there were potential alternatives to capture this rich protein source, including conventional breeding. Why not perform crosses and screen for cotton that is gossypol free? This is very doable from a breeding perspective, and in fact was successfully done and the resulting plants were shown to be gossypol free; but these plants were also extremely susceptible to fungi and insects and while gossypol free, entire fields were lost! This was a costly lesson to show that gossypol confers protection from insect parasites and fungal pathogens. But is there an alternative strategy? This is where the power of biotechnology provides recourse.

(This following work was done by Dr. Keerti Rathore and colleagues in the Borlaug Center). Briefly, the biochemical pathway for gossypol biosynthesis in plants is known. Employing a synthetic biology approach, Rathore used a regulatory element that directed genes specifically to the seed ("tissue specific"). When this element was coupled to the enzyme making gossypol and turned off by Virus Induced Gene Silencing (VIGS), the enzyme was inactivated but only in the seed, thus yielding gossypol free cottonseed. The rest of the cotton plant still made gossypol and thus was protected from pathogens. Importantly, yields were maintained. These transgenic plants are thus gossypol free in the seed and the rest of the cotton plant synthesizes normal levels of gossypol and is protected from biotic stress. Gossypol levels in these plants are well below FDA recommendations and several patents have been issued. Thus, the potential of cottonseed in contributing to the nutrition requirements of the burgeoning world population may be realized. Thus, in this particular example, this research is impossible without the availability of the new biotechnology tools, which were the only alternative.

**Banana**

The work to be summarized was part of a joint collaboration between Dr. Marty Dickman (IPGB-Borlaug Center-Texas A&M) and Professor James Dale (Queensland Institute of Technology in Australia).

Banana is grown throughout the tropical and subtropical regions of the world and is a key staple food in many developing countries, as well as a source of income for subsistence farmers. Diseases are major constraints wherever banana is produced. The vast majority of edible bananas grown today are selections that have not undergone improvement through conventional breeding due to the important and key fact: they are essentially **sterile** and thus an effective breeding/genetic program is not a viable option. Thus, a "molecular breeding" approach is widely considered the most promising strategy to generate disease resistance and stress tolerance in this crop, almost by default.

Diseases reduce yields by debilitating plants and reduce the quality of fruit before and after harvest. Diseases range from esthetic problems that lower the marketability of the harvested product to lethal constraints that devastate local or regional production. Disease is the key reasons that banana-breeding programs have been created worldwide. The major diseases of banana are due to fungi; in particular fungi that secrete toxic metabolites. The Dickman lab studies cell death and has identified genes that are cytoprotective (anti-death). This was done using bioinformatics and was based on structural predictions that would not have been noticed by conventional screens. As a result we can modulate cell death transgenically and have shown that if we can prevent cell death (as in this case), the pathogen is unable to kill host plants and acquire nutrients; these fungal pathogens eventually die of starvation and the plant is protected. We have performed molecular breeding directed field studies in Australia where bananas are grown commercially and have selected several promising lines.

Bananas also illustrate a common scenario in modern agriculture with respect to plant diseases; the so-called "Arms race." When large acreages of genetically uniform disease resistant plants are grown, selective pressure often results in the pathogen adapting and overcoming the formerly resistant plant. Breeders then come in and breed against these new strains, and an arms race is on as has occurred throughout history. This has occurred in banana as well as wheat. This new fungal (killer) strain is very aggressive, is spreading and there is no genetic resistance. Growers are concerned and rightfully so. In the past, these diseases have led to starvation and even death in developing countries. We are currently testing our lines against this strain (race), and we are cautiously optimistic these transgenic plants will provide resistance.

The Dale lab is also involved with bio-fortification in banana by transgenically increasing carotenoid (Vitamin A) levels in banana in an analogous situation to the Golden Rice situation. Deficiency of Vitamin A causes blindness in young children. According to the World Health Organization, dietary vitamin A deficiency (VAD) compromises the immune systems of approximately 40 percent of children under the age of five in the developing world, greatly increasing the risk of severe illnesses from common childhood infections, and causing hundreds of thousands of unnecessary deaths among them. The Dale lab has been remarkably successful ingenerating banana with biologically relevant levels of Vitamin A; tests for human consumption and allergens of banana are in progress.

## II. PHYTOBIOME

The plant microbiome ("Phytobiome") is a relatively new field of study with intriguing potential applications that are in the early stages of development. The phytobiome is analogous to probiotic studies in humans (e.g. gut microbiome). The plant microbiome is an assemblage of microbes living in, on and around plants. These biomes function as a community of microorganisms with predictable compositions and are partners for life. Importantly microbial endophytes (resident internal microflora) involved with agricultural plant hosts have recently been shown to confer or are correlated with enhanced and in some cases remarkable positive agronomic traits (e.g., drought tolerance, disease resistance and others). Phtytobiomes can influence or be influenced by plants or the plant environment. Key questions include:

1) Can these relationships be tapped to improve crop health, safety, quality and productivity?

2) Can we develop microbes that reduce effects of drought, flood, and salinity, or develop microbes to enhance root growth hormonally – more and deeper roots! This is an opportune time for these studies as robust tools are now available (especially sequencing, "omics" and various computational approaches). We can address a number of questions previously unable to be asked about microbes in the environment—including who, how, what and why with tremendous precision, impact and accuracy often with unexpected results. Remember >99% of the soil meta-genome is completely uncharacterized and in most cases cannot be grown without a plant host. Lots of untapped resources and commercial opportunities exist in this realm of research.

3) Can we breed plants that select for a beneficial microbiome? (e.g., disease is associated with shifts in microbiome composition.)  Such shifts can be diagnostic for disease. (e.g., take all of wheat and suppressive soils). Microbes have been shown to reduce effects of drought, flood, and salinity. Microbes form biofilms, reducing ion movement into the plant. More work is needed to establish the relevant underlying mechanisms.

4) Do plants control their microbiome composition?  It appears they do, based on research conducted by Dr.  R. Rodriguez. Dr. Rodriguez initiated his work in Yellowstone Park, surveying and characterizing thermotolerant plants. He discovered that all heat tolerant plants that were studied had a specific, consistent associated fungus in the roots. Sensitive, non thermotolerant plants did not. Thus, thermotolerance correlated with the presence of the fungus. Similarly, his research in Seattle looked at plants growing in salt water, on the beach and on a hill overlooking the beach, and again he identified fungi that conferred the "proper" stress tolerance. Finally, in Oklahoma, during a melon study, he identified fungi that conferred disease resistance in melons.

**III. GENOME EDITING (CRISPR/Cas9)**

Briefly, genome engineering involves generating targeted alterations to the genome of an organism or cell. This can result in deletion insertions or modification. Targeted genome editing has recently exploded with significant experimental potential and power in both model and crop plants. As several limitations have been overcome, ease of use and affordability has occurred. The recent advances in several genome editing technologies, including the ability to specifically customize these engineered nucleases, particularly, the emergence of the CRISPR/Cas system (Clustered Regularly Interspersed Short Palindromic Repeats) has fueled considerable interest in the genetics plant improvement as well as in the biomedical arena. With particular emphasis on plants; two important advances include multi-plexing (addition of several genes in one experiment), and breeding. Breeders now have a powerful, high throughput tool to generate variation; the cornerstone of breeding. These features are likely to change the face of contemporary breeding approaches.

This remarkable ("Game changing") technology now provides the ability to customize and generate informed genetic modifications for **any** number of plant phenotypes. Plants are in the early stages of this technology with the bulk of the work thus far involving proof of concept and establishing experimental parameters. The clear potential awaits rigorous testing, the promise and potential are formidable all of which is likely the tip of the iceberg.

**Conclusions**

In closing, I want to reiterate that a new Green Revolution is necessary to meet the challenges that lie ahead. As the population increases, resource constraints increase, and climate becomes less predictable, the need for more food continues to rise. We must take advantage of all the tools available to address this need. Significant discoveries/paradigm shifts are often unexpected or unintended (e.g., penicillin, CRISPR) and support for fundamental research support is critically important to create opportunities for these discoveries and to provide new tools to address these problems. Research allows us to understand the mechanisms, how the technology works, and to optimize, improve, and commercialize new technologies. To commercialize an agricultural product require lots of time and lots of resources. These traits are often outside the comfort zone of a professor, and private companies are often far better equipped for high throughput scaling up.  User friendly commercialization procedures could encourage increased development of commercial potential.

This is an exciting time for life sciences research.