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Editorial overview: Growing the future: synthetic biology in plants

Sarah E O'Connor and Thomas P Brutnell



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For a complete overview see the [Issue](#) and the [Editorial](#)

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Sarah E O'Connor

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Sarah E O'Connor The O'Connor group is interested in elucidating and manipulating natural product pathways. They are particularly interested in alkaloid natural products, with an emphasis on alkaloid pathways derived from medicinal plants. Recent research has focused on the identification of key enzymes in the monoterpene indole alkaloid pathway, and exploiting these enzymes to make new-to-nature products.

Thomas P Brutnell

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Thomas P Brutnell The Brutnell lab is focused on understanding photosynthetic differentiation and, in particular, identifying the transcriptional networks that drive C4 photosynthetic development. Applications of this research include improving photosynthetic efficiencies in emerging bioenergy feedstocks such as Miscanthus and switchgrass, as well as improving yield in existing C4 crops such as maize, sorghum and sugarcane. The lab is also working with a large international consortium to engineer C4 traits into C3 grasses.

Plants have played a fundamental role throughout the course of human history, providing us with food, shelter, clothing, medicines and fuel. Indeed, the origins of nearly all civilizations can be traced to the domestication of crops that transformed low yielding wild relatives of wheat, rice, maize or beans into staples for society. While yield improvements have traditionally been obtained through breeding — artificial selection on natural variation, we are now entering a new era of directed manipulation of plant genomes. The field of synthetic biology holds great promise to combine engineering principles with a deep understanding of biological mechanisms, to reprogram living systems. Unfortunately, the field of synthetic biology has been comparatively slow to develop in plants when compared to the progress made in microbial systems. Given the complexity of plants — organisms that are multicellular, developmentally complex, with large genomes and complex regulatory mechanisms — this is perhaps not surprising.

In this issue, we present a series of articles that collectively illustrate how far we have come in the development of synthetic biology approaches that are specifically tailored to plants and plant biology. In the last 5 years, the field of synthetic biology has exploded, and the coverage represented by this selection of articles is therefore wide ranging.

We start by presenting new technologies that impact the expression and silencing of genes in plants. [Birchler and coworkers](#) describe their pioneering work exploring how artificial chromosomes can be incorporated into plants in their article “Engineered minichromosomes in plants.” While this work is still in the early stages of application, the power of synthetic chromosome technology could potentially provide many advantages over other methods of genetic modification, including the installation of multiple metabolic pathways onto a single chromosome. [Lomonosoff and coworkers](#) describe the advantages and applications of transient expression, a system for rapid protein expression in plants, in their article “Transient expressions of synthetic biology in plants.” The authors pay particular attention to the use of virus-derived transient expression systems to express active enzymes. There have also been a number of recent advances in genome editing of plants. In [Bogdanove's](#) article “Principles and applications of TAL effectors for plant physiology and metabolism” the advantages and disadvantages of TAL effectors for DNA targeting in plants is discussed. [Bogdanove](#) compares and contrasts this system with the recently reported CRISPR/Cas9 method of genome editing. At the heart of nearly all gene network reconstruction is the ability to employ robust, rapid and inexpensive methods for DNA assembly.

In [Parron's](#) article "DNA assembly for plant biology: techniques and tools" the most recent methods for DNA assembly are discussed. While these techniques are not limited to plant biology applications, they are crucial for the generation of the large constructs that are required for the synthetic biology technologies applied to plants.

In addition to describing some of the emerging tools for systems engineering in plants, several articles discuss the great potential in engineering plant biosynthetic enzymes and pathways. These enzymes are the building blocks that form the basis for all synthetic biology approaches impacting plant metabolism. In "The chemical logic of plant natural product biosynthesis" [Sattely and coworkers](#) provide a chemical perspective that broadly groups metabolic pathways into specific reactions and functional groups. The chemical themes that underlie a range of plant pathways are highlighted: namely, scaffold generating steps that draw on a limited set of chemistries, and tailoring reactions that derivatize these common scaffolds. [De Luca and coworkers](#) outline the process by which biosynthetic enzymes are discovered in "Making iridoids/secoiridoids and monoterpenoid indole alkaloids: Progress on pathway elucidation." Until recently, enzyme identification was the primary bottleneck in all plant metabolic engineering efforts, but recent developments in sequencing technologies and bioinformatics have opened the door to understanding biochemistries in plants that are less tractable to genetics. A good example is the cytochrome P450 family of monooxygenases. These versatile enzymes catalyze an extraordinary range of chemical transformations and are present in nearly all plant metabolic pathways. [Werck and coworkers](#) describe these enzymes, and their potential in metabolic engineering, in the article "Cytochrome P450-mediated metabolic engineering: current progress and future challenges." It is essential to note that plants exploit their complex developmental biology to spatially restrict the activity of enzymes through compartmentation in several organelles such as mitochondria, chloroplasts and peroxisomes. [Gourdavault and coworkers](#) describe how metabolic enzymes are localized, and the implications of such localization, in their article "A look inside an alkaloid multisite plant: the *Catharanthus* logistics."

We also include a series of articles describing translational applications of synthetic biology, historically called metabolic engineering, though this work is now typically grouped under the synthetic biology umbrella. Engineering of terpenes, anthocyanins and lipids are described. [Giuliano and coworkers](#) describe how carotenoids can be engineered into crop plants in their article "Metabolic engineering of plant carotenoids: genomics meets multi-gene engineering". [Martin and coworkers](#) give a detailed account of anthocyanin biosynthesis, and the implications that this knowledge has for engineering these compounds in food sources to improve human health. [Napier and](#)

[coworkers](#) describe the challenges and successes of engineering lipid composition in plants with applications to improve the nutritional content of plants or biofuel potential in their article "Understanding and manipulating plant lipid composition." The applications can also be extended to plant protection. In "Prospects of genetic engineering for robust insect resistance", [Pickett and coworkers](#) describe how metabolic engineering efforts can impart insect resistance to plants.

While plants can be engineered to (over) produce metabolites, plant metabolic pathways can also be reconstituted in microbes. This approach may prove a cost-effective strategy to produce high-value plant products in easy to grow microbes such as yeast. [Pfeifer and coworkers](#) describe the successes achieved in such efforts in their article "Heterologous production of plant-derived isoprenoid products in microbes and the application of metabolic engineering and synthetic biology."

Finally, we conclude with several articles that focus on how plant phenotypes are shaped by Nature. [Kliebenstein](#) highlights the power of natural variation in "Synthetic Biology of Metabolism: Using natural variation to reverse engineer systems." What we now know about the genetic control of natural variation in plant metabolism suggests that successful engineering must incorporate information about many genes before an introduced pathway can be optimized. Observations from natural variation therefore provide inspiration for more sophisticated approaches in synthetic biology. In "Dosage, Duplication, and Diploidization: clarifying the interplay of multiple models for duplicate gene evolution over time," [Pires and coworkers](#) describe how dosage balance influences the effects of gene duplications, gene copy number variations, and epigenetic factors. The absolute and relative dosage of a given gene has a powerful impact in shaping the phenotype and fitness of the plant. Thus, the most sophisticated approaches in synthetic biology must also incorporate these factors. Epigenetic modifications that are observed in nature are another crucial aspect that must be considered in plant engineering efforts. Given the links between epigenetic changes and improved photosynthesis, [Peterhansel and coworkers](#) discuss the feasibility of altering the epigenetic code to enhance photosynthesis in their article "Can we learn from heterosis and epigenetics to improve photosynthesis?". The authors raise an intriguing direction of future synthetic biology research: engineering a hybrid-like state of epigenetic modifications into the genome of an inbred line.

Usage of GM (genetically modified) crops has been limited due to challenges in social acceptance. Development of synthetic biology approaches in plants will ideally circumvent similar controversies. Given the prospect of serving a population of 7 billion (and growing) we ignore the extraordinary opportunities that synthetic biology offers at our own peril.