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Editorial overview: Plant synthetic and systems biology

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The vision to rationally engineer organisms has been a biotechnology goal that dates back several decades [1,2]. Advances of the post-genomic era and the highly resolved bioanalyses that came with advanced systems biology [3] gave rise to synthetic biology, i.e. the rational engineering and control of reprogrammed cellular behavior [2]. Synthetic biology can be seen to originate in the technical and information advances of the late last century and to take a strong foothold in the first years of the new millennium [2]. In this vein, mathematical model-based designs enabled simple genetic circuits, such as toggle switches and oscillators, in *E. coli* which remains the most feasible organismal chassis of synthetic approaches [4,5]. These initial successes laid the ground for engineered microbial systems for example the use of *Saccharomyces cerevisiae* (baker's yeast) for the production of plant-derived pharmaceuticals, such as the anti-malaria drug precursor artemisinic acid [6] or the primary drugs used for pain management plant opioids [7]. Equally important and global-scale goals of synthetic biology are efficient biofuel production in both non-photosynthetic [8] and photoautotrophic microorganisms [9].

Compared to microbe biotechnology plant synthetic biology is at an embryonic stage yet rapidly evolving. Synthetic approaches strongly impact plant biotechnology. In this compendium we follow up on an earlier status report [10] and aim for an "on the fly" updated snapshot of current developments. Contributions highlight novel designs of carbon assimilation as basis of global plant productivity. They discuss *in silico*, experimental and analytical technologies that enable rational engineering of advanced multi-component genetic circuits in oxygenic photosynthetic systems and allow direct sustainable production. This compilation contains examples of implemented or imminent applications in photosynthetic hosts that range from seed plants through algae to cyanobacteria and even include the tuning of *E. coli* towards novel paths of carbon assimilation. We cover traditional and novel plant specific targets of biotechnology that will benefit from or can now be tackled by the emerging engineering schemes available within the umbrella of plant synthetic biology.

Zarzychki and Erb provided a state-of-the-art overview of the massively abundant enzyme RuBisCO including structural, physiological, microbiological and phylogenetic data to speculate on a range of evolutionary aspects of RuBisCO based carbon dioxide fixation. They cover the potential of RuBisCO in what they term the RuBisCOsome — a range of assembly and interacting factors which serve to improve the functionality of the enzyme. Synthetic approaches to overcome evolutionary constraints on RuBisCO are discussed that may allow the rewriting or even ultimate replacement of this highly successful enzyme.

By contrast, the paper of **Cotton et al.** discusses an alternative route of carbon assimilation employed by bacterial pathways which convert carbon dioxide to formate or carbon monoxide. They compare and contrast this pathway with that in which RubisCO operates on the basis of the kinetic properties of the constituent enzymes and the subsequent resource efficiencies. They conclude that fixing carbon dioxide after conversion to formate may even have an advantage in terms of biomass accumulation in spite of the thermodynamic barrier of carbon dioxide reduction.

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Prokaryotes are the obvious hosts of choice to build artificial biological systems. **Hagemann and Hess** review recent advances in systems and synthetic biology of cyanobacteria, the perhaps most ancient and best understood models of oxygenic photosynthesis. The cyanobacteria chassis can host modifications by standardized molecular tools, so called BioBricks (http://parts.igem.org/Main_Page). Plant and specifically chloroplast research can build on applications that are tested in a photosynthetic prokaryote. Cyanobacteria may ultimately enable direct production of biofuels and chemicals from CO_2, light and sea water without competing crops food production.

Inherent to the re-design of carbon assimilation for direct production are modeling strategies. In particular genome-scale modeling to identify targets for synthetic biological improvement of photosynthetic organisms is discussed by **de Oliveira Dal'Molin and Nielsen**. They describe how genome-scale models are now being generated beyond single cells for complex tissues or whole plants to reflect organismal functions. They highlight examples wherein post-genomic datasets from multiple tissues are integrated to facilitate data interpretation.

Next to *in silico* procedures a set of novel experimental technologies are necessary for successful synthetic plant biology. A fundamental prerequisite is the establishment of genome editing techniques. In her review **van Eck** provides a comprehensive summary of the development of genome editing techniques for plants. She argues that these techniques in parallel to the availability of sequenced genomes lead to effective strategies for altering plant genomes in a DNA site-specific manner. Whilst this is a rapidly advancing area and is the subject of many recent reviews, e.g. [11–13], the article of **van Eck** discusses how these approaches will ultimately enable synthetic biology in crops that are currently underutilized species.

Genome editing will greatly enhance our ability to improve nutritional and medicinal properties of our cultivated plants. Based on the advances of genome editing and of stacking genetic modifications **De Lange et al.** describe the use of genetic circuits for the engineering of crop plants. Synthetic genetic circuits are designed sets of genetic parts that combine both, coding and regulatory functions for the purpose of establishing a new desired function [1,2]. The genetic circuit concept was demonstrated in microbes [4,5] and is currently considered for plant biotechnology. The authors cover plant specific aspects of circuit design, balance planed and random approaches and suggest prototyping for transfer to crops. Socio-cultural aspects of customer acceptance and required regulatory procedures are discussed.

Key to the establishment of new genetic circuits and contained bio-synthetic units is plant organelle transformation. **Fuentes et al.** highlight recent engineering progress based on alternative selection after plastid transformation. Transplastomic engineering was recently combined with modifications of the nuclear genome. The limits of either technology alone are overcome by combinatorial transformation to tap photosynthetic reducing power and to access new and edible plant hosts. Advances are exemplified by successful plastomic and combinatorial engineering of the synthesis of dhurrin, astaxanthin and the anti-malaria drug precursor artemisinic acid.

Towards a more efficient design of gene regulatory cassettes **Lee and Bailey-Serres** argue that synthetic plant biology requires insight into spatially and temporally resolved regulatory steps of transcription and translation that were previously not accessible. They describe the multiplexing of multi-scale gene regulation assays that combine nucleus- and