Cyanobacteria as a solar-fueled chassis to make a wide variety of compounds

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Photosynthesis is the only natural process that uses solar energy to generate both reducing power (NAD(P)H) and cellular energy (ATP) that are used in turn for carbon fixation and for generation of a wide variety of compounds. This enables photosynthetic organisms to generate compounds of interest from just CO_2, sunlight and water, thus providing an advantage, in principle, over heterotrophic systems, although without added sugar phototrophs typically do not reach the same cell density. Metabolic engineering can further increase the number of compounds made, and maximize the amount of selected desired products. Prokaryotes are generally more accessible to metabolic engineering efforts than algae or plants are, due to the reduced number of compartments, more facile transformation, and the simpler genetic make-up. Cyanobacteria are prokaryotes that are the evolutionary ancestor to chloroplasts and that essentially can be viewed as free-living chloroplasts.

We utilize a cyanobacterium, *Synechocystis* sp. PCC 6803, that is an excellent model system and that can also grow well in outdoor photobioreactors. The organism is amenable to targeted gene deletions and insertions, and has a flexible metabolism in that it can grow photoautotrophically or can use glucose as a carbon source. We have introduced genes to enable, for example, the production of free fatty acids or isoprene. The products are readily excreted and thereby it is not necessary to harvest the cyanobacteria and extract the product: one can simply devise methods to harvest the excreted product. Typically it does not suffice to introduce a pathway that enables production of the desired compound as the yield needs to be optimized. This optimization may be done via upregulation of the desired pathway, inhibition of competing pathways, etc. However, insight into regulatory mechanisms of the cell often limits our ability to approach optimal yields. Nonetheless, cyanobacteria provide an excellent vehicle to make a wide range of "green" chemicals essentially from CO_2 and water. Examples of production of compounds of commercial interest in cyanobacteria will be discussed.