



6TH BCNP
Brazilian Conference
On Natural Products
XXXII RESEM



Federal University of Espírito Santo
Vitória – ES/Brazil
November 05–08/2017

THE ULTIMATE WAY TO “GO GREEN”: CHANNELED LIGHT-DRIVEN PRODUCTION OF STRUCTURALLY COMPLEX DITERPENOIDS

Birger Lindberg Møller

Plant Biochemistry Laboratory, Center for Synthetic Biology “bioSYnergy”, University of Copenhagen, Thorvaldsensvej 40, DK-1871 Frederiksberg C, Copenhagen, Denmark.
blm@plen.ku.dk

With 12,000+ known structures, diterpenoids are a prime example of bio-active natural products produced by plants. Many are used as highly valuable pharmaceuticals, fragrances, natural plant growth promoters, food ingredients such as flavors or as colorants and spices. Unfortunately, they are typically produced in minute amounts in plants and their structural complexity render them difficult to prepare from fossil resources using organic chemical synthesis. Terpene synthases, cytochrome P450s and acyl transferases are key multienzyme families involved in diterpenoid synthesis. Using mass spec based imaging of the target plant tissue, tracer studies, single cell-type based metabolomics and transcriptomics, functional characterization of gene candidates using transient expression in tobacco and LC-MS-NMR based structural identification, elucidation of even highly complex biosynthetic pathways is now possible within a reasonably short time frame. Terpenoid metabolism is modular right from assembly of the C₅ building blocks to the final structurally complex diterpenoid. Using the approaches of synthetic biology for combinatorial biosynthesis, the functional modules may be assembled in new combinations to expand the landscape of diterpenoid structural diversity into new-to-nature structures. Our elucidation of the entire pathway for forskolin will be presented. Forskolin is a cyclic AMP booster approved for treatment of glaucoma but also used as a weight loss aid. The forskolin pathway is being used as test model system for large scale light driven production of high value diterpenoids following targeting of the pathway to the photosynthetic thylaloid membrane using cyanobacteria or moss as photosynthetic production hosts grown in contained photo-bioreactors.

Realization



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