Bioprocess optimization for bacterial synthesis of natural products

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In the last decade, industrial biotechnology has emerged as a successful alternative for the production of chemicals and materials which are traditionally chemically derived from fossils. This sustainable production of bio-chemicals and materials through microbial fermentation from renewable resources, consequently contributes to establishing bio-based economy and achieving low carbon green growth.

Recent advances in metabolic engineering combined with systems biology and synthetic biology opened the route to development of microbial hosts and bioprocesses for the efficient production of natural products (i.e. secondary metabolites). Before, these natural products were being directly extracted from plant materials or chemically synthesized through a tedious, environmental unfriendly, multi-step process yielding low titers. Novel methods, such as multivariate modular metabolic engineering (MMME) allows the systematically engineering of microbial hosts for the synthesis of secondary metabolites boosting the rapid construction of superior strains. An additional challenge in designing bioprocesses for these natural products comes with the inherent properties of these components (e.g. a lot of these components are volatile).

Here we will demonstrate the development of a bioprocess for terpenoids, a class of secondary metabolites consisting of many chemicals [illegible]. We will show how applying MMME can result in a superior strain synthesizing kaurene, the precursor of gibberellin. Optimizing the bioprocess design resulted in doubling of the kaurene titers. These titers improved even further by optimizing fermentation conditions at larger scale.