

# **Technology Offer**

**Strain construction and screening library for natural products** Ref.-No.: 0706-6410-IKF

Natural products from plants and microorganism are potent bioactive molecules that have been widely used in medicine, agriculture, food industry and cosmetics. Increased awareness of the environmental and health concerns of consuming chemically synthesized products has led to a rising demand for natural products that are greener and more sustainable. Moreover, the increasing frequency of antibiotic-resistant infections clearly demonstrates a continues need for novel antibiotics. Despite the importance of natural products, industrial-scale production has been hampered mainly due to the low yield and high costs of the bioprocesses.

### Technology

Scientists from the Max-Planck-Institute for Terrestrial Microbiology have identified a method for finding global regulators in order to induce or increase the production of target secondary metabolites. They could show that the deletion of important global regulators like the RNA chaperone Hfq, its sRNA partner ArcZ, the DNA methyltransferase Dam1 or the cAMP synthase CyaA leads to a loss of all natural products while hardly affecting bacterial growth. In a mutant background of such global regulators, the natural promotor of a biosynthetic gene cluster is exchanged to an inducible one, leading to the production of the desired natural product in high yields and in the absence of any unwanted side products.

The scientists could also show that a "all-in-one" CRISPR/Cas-based single plasmid is sufficient to delete or inactivate a global regulator and to activate a biosynthetic gene cluster at the same time. Using this method, they were able to obtain high production titers of up to 336 mg/L of the high value compound safracin B, a semisynthetic precursor for the anti-cancer drug ET-743. Their existing screening library comprises 200-300 strains which produce novel natural products in high yields.

#### **Advantages**

- comprehensive strain collection to screen for novel biologically active natural products
- "all-in-one" strain construction which allows high production titer of desired natural products in the absence of unwanted side products

## Patent Information

A patent application was filed on June, 9th 2023.

#### Publications

Rill et al., *Microbial Cell Factories* 2024. <u>https://doi.org/10.1186/s12934-024-02363-8</u> Bode et al., *Angewandte Chemie* 2019. doi: <u>10.1002/anie.201910563</u>

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