Tutoring for nature: Production of valuable nootkatone with yeast

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acib researcher Tamara Wriessnegger is manipulating a bioreactor with yeast producing valuable nootkatone. Credit: acib

New method allows production of expensive grapefruit aroma Nootkatone biotechnologically from cheap sugar using a 'turbo-yeast.' The versatile, healthy and tasty substance is used in soft drinks, pharmaceutical products or even as an insect repellent.

The Austrian Centre of Industrial Biotechnology (acib) uses the positive aspects of synthetic biology for the ecofriendly production of a natural compound. The challenge of the biotechnologists Tamara Wriessnegger and Harald Pichler in Graz was to produce Nootkatone in large quantities. The substance is expensive (more than 4000 USD per kilo) and can be found only in minute quantities in grapefruits. At the same time the need is great, because Nootkatone is used as a high quality, natural flavoring substance in millions of liters of soft and lifestyle drinks, as a biopharmaceutical component or as a natural insect repellent .

"We have installed new genetic information in the yeast *Pichia pastoris*, so that our cells are able to produce Nootkatone from sugar", says acib researcher Tamara Wriessnegger. The genome of the yeast cells has been extended with four foreign genes derived from the cress *Arabidopsis thaliana*, the Egyptian henbane *Hyoscyamus muticus*, the Nootka cypress *Xanthocyparis nootkatensis* and from baker's yeast *Saccharomyces cerevisiae*. Ultimately, the aroma found in one grapefruit leads to millions of liters of tasty juice.

With the help of the new genes the yeast is capable to synthesize the high-prized, natural flavor (more than 4000 euros per kilo) in a cheap way and in useful quantities from sugar (one euro per kilo). Nootkatone is an important substance for the food, pharmaceutical and chemical industries, says Harald Pichler. As an insecticide it is effective against ticks, mosquitoes or bedbugs. In the medical field, the substance has shown activity against cancer cell lines. In cosmetics, people appreciate the good smell, in soft drinks a fine, subtle taste. Because the natural

sources cannot meet the demands, the acib method replaces chemical synthesis - an energy-consuming and anything but environmentally friendly process. The common biotech variant via Valencene and a chemical synthesis step is less ecofriendly, more difficult and expensive. Pichler: "With our method, the important and expensive terpenoid Nootkatone can be produced industrially in an environmentally friendly, economical and resource-saving way in useful quantities."

Synthetic biology could be of vital importance to humanity, as Artemisinin shows. Thanks to this substance malaria is curable. Unfortunately, it could be found only in tiny quantities in the sweet wormwood - until the US researcher Jay Keasling was able to transfer the appropriate production route from the plant in bacteria. With these "synthetic" organisms the active ingredient is produced at lower costs.

More information: The acib research results were published in the journal Metabolic Engineering: DOI: 10.1016/j.ymben.2014.04.001

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