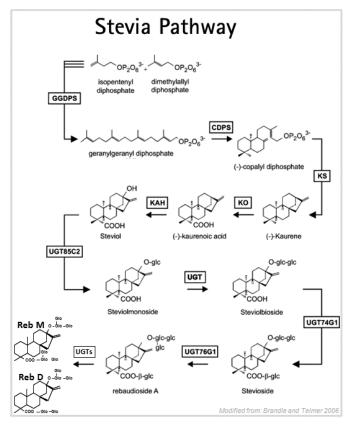
## METABOLIC ENGINEERING OF SACCHAROMYCES CEREVISIAE TO HARNESS NATURES VALUABLE COMPOUNDS

Christian Nyffenegger, Evolva christiann@evolva.com Ângela Carvalho, Evolva Klavs Riishede Hansen, Evolva Esben Halkjær Hansen, Evolva Jean Amick, Evolva Giovanni Salerno, Evolva Jørgen Hansen, Evolva

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Nature contains a treasure trove of small molecule ingredients that can improve health, wellness and nutrition. However, most of these ingredients have "issues": the organism that makes the compound of interest is too rare, too hard to grow or does not make enough of it. Hence, the ingredient is not available at the right quality, the right price nor the necessary amount. These issues need to be solved in order to allow a larger society having access to these valuable ingredients in a sustainable manner at low costs. Evolva is leader in metabolic engineering of yeast for the production by fermentation of a diverse array of small molecule ingredients. The small molecule ingredients introduced to the market by Evolva include Resveratrol, Nootkatone, Valencene and Vanillin. Evolva and its commercial partner will launch the next-generation stevia sweetener EverSweet<sup>™</sup> in 2018. All of these molecules are produced in a sustainable, reliable, cost-effective production at consistent quality by fermentation of engineered yeast strains, using abundant, inexpensive raw materials. Of particular interest to Evolva are the terpenes, which are known to work in a wide range of high value applications including sweeteners, flavors and fragrances, personal care, as well as human and animal health products. In spite of proven efficacy, there has been relatively little commercial development of terpene-based ingredients, mostly due to their high production cost. Here, we will present a number of terpene-based Evolva ingredient projects such as e.g. the stevia pathway, which use Evolva's technology platforms, allowing us to produce these ingredients in an efficient and sustainable way.



Biosynthesis of steviol glycosides via the mevalonate pathway. The geranyl-geranyl-diphosphate-synthase (GGDPS) catalyzes the formation of the diterpene precursor geranylgeranyl-PP, which is converted in subsequent steps to steviol. Steviol is then glycosylated by the action of glycosyl-transferases, giving rise to the premium steviol-glucoside sweeteners RebD and RebM, respectively.