



Yeast has been engineered by Ginkgo BioWorks to produce a fragrance ingredient.

## BIOENGINEERING

# Synthetic-biology firms shift focus

*Switch to food and fragrances risks consumer rejection.*

BY ERIKA CHECK HAYDEN

Plain old vanilla doesn't impress Neil Goldsmith, chief executive of Evolva, a synthetic-biology company based in Reinach, Switzerland. This year, his company will release a product that has been created by genetically modified yeast that converts sugars to vanillin. It will be the first major synthetic-biology food additive to hit supermarkets.

The product marks a shift for the industry, which has typically focused on the synthesis of drugs and commodities such as biofuels and rubber. Now, synthetic-biology companies are turning to 'fine chemicals': food and fragrance ingredients that command high prices in small batches. "The products take less time to develop, they take less money to develop, and they're much less risky," says Goldsmith.

But the products may carry a different type of hazard: consumer rejection. By creating products designed to be ingested or put on the body, synthetic-biology companies are starting to attract the attention of groups that oppose the use of genetically modified (GM) organisms. But regulations governing the use and labelling of GM organisms do not apply to fermented ingredients, because the organisms used to make them are not present in the final products.

Synthetic-biology companies are already marketing a few fine chemicals: engineered yeast has been used to make valencene and nootkatone, which provide the aroma of oranges and grapefruits, respectively, in perfumes and cosmetics. And at least five high-profile fine chemicals are scheduled to be released this year. Biofuels and commodity materials are still a mainstay, but firms are moving quickly to tap into an estimated US\$20-billion market for fine chemicals, says Mark Bünger, research director at Lux Research, headquartered in Boston, Massachusetts, which tracks the industry. "We're barely scratching the surfaces of the chemicals for which we already know there are markets," he says.

Synthetic-biology companies have found it hard to break into established commodity markets with new biofuels and petroleum-based products, because businesses trade in high volumes and low prices. Also, the price of oil has not risen as high as some biofuels advocates had predicted. "The big challenge with making commodity chemicals is that those things are really cheap, and you have to straight-up compete on price,"

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says Reshma Shetty, co-founder of Ginkgo BioWorks in Boston, which has signed deals with unnamed partners to make six fine-chemical ingredients. These ingredients can command prices of the order of \$10–10,000 per kilogram, compared with around \$1 per kilogram for biofuels.

There are other pluses. Synthetic biologists can fine-tune their product profiles to be more palatable. That is a big draw for products such as stevia, a no-calorie sweetener extracted from a leafy green plant native to South America. The sweetness comes mainly from rebaudioside compounds such as Reb A and Reb D. But the most abundant of these — Reb A — becomes bitter in large quantities, whereas the sweeter ones, such as Reb D, are present in such small amounts that it would be too expensive to extract them from stevia plants in the mass quantities needed, for example, to sweeten soft drinks. So Evolva is trying to engineer a yeast that would ferment a better-tasting stevia based on the sweeter Rebs. "What we hope this means is that you can go to having a cola product based on, let's say, Reb D, where you can get the taste right and the economics in units affordable to the consumer," Goldsmith says.

Another advantage of the bioengineering route is that these additives can be swapped for those extracted from nature and still legally be called natural because they are made by living organisms (typically, yeast). And because it is added to food after the yeast has been removed, the ingredient itself need not be labelled in any particular way. As long as it is equivalent to one of the many used in the food industry that are generally recognized as safe, it can be added to foods without any regulatory review.

How consumers will respond to these products is unclear. Already, Friends of the Earth US, an environmental group based in Washington DC, is asking consumers to sign an online petition calling for food companies not to use synthetic-biology-derived vanillin in ice cream.

Some companies are positioning themselves for the coming battle. Solazyme, based in South San Francisco, California, modifies algae to produce oils that are added to cosmetics sold by the international beauty chain Sephora. A spokesperson says that its products "are made naturally by microalgae".

Carolyn Fritz, chief executive of Allylix in San Diego, California, takes a different tack in trying to head off concerns. Her company uses yeast to make terpenes — organic chemicals that can be extracted from plants for use in fragrances and foods. She points out that one of the main synthetic-biology processes, using the fermentation powers of yeast, is something that should be familiar to thirsty consumers. "We're using a process very similar to that used to make beer, wine and lots of other products," she says. ■