CASE STUDY

TWIST BIOSCIENCE

For the Love of Beer

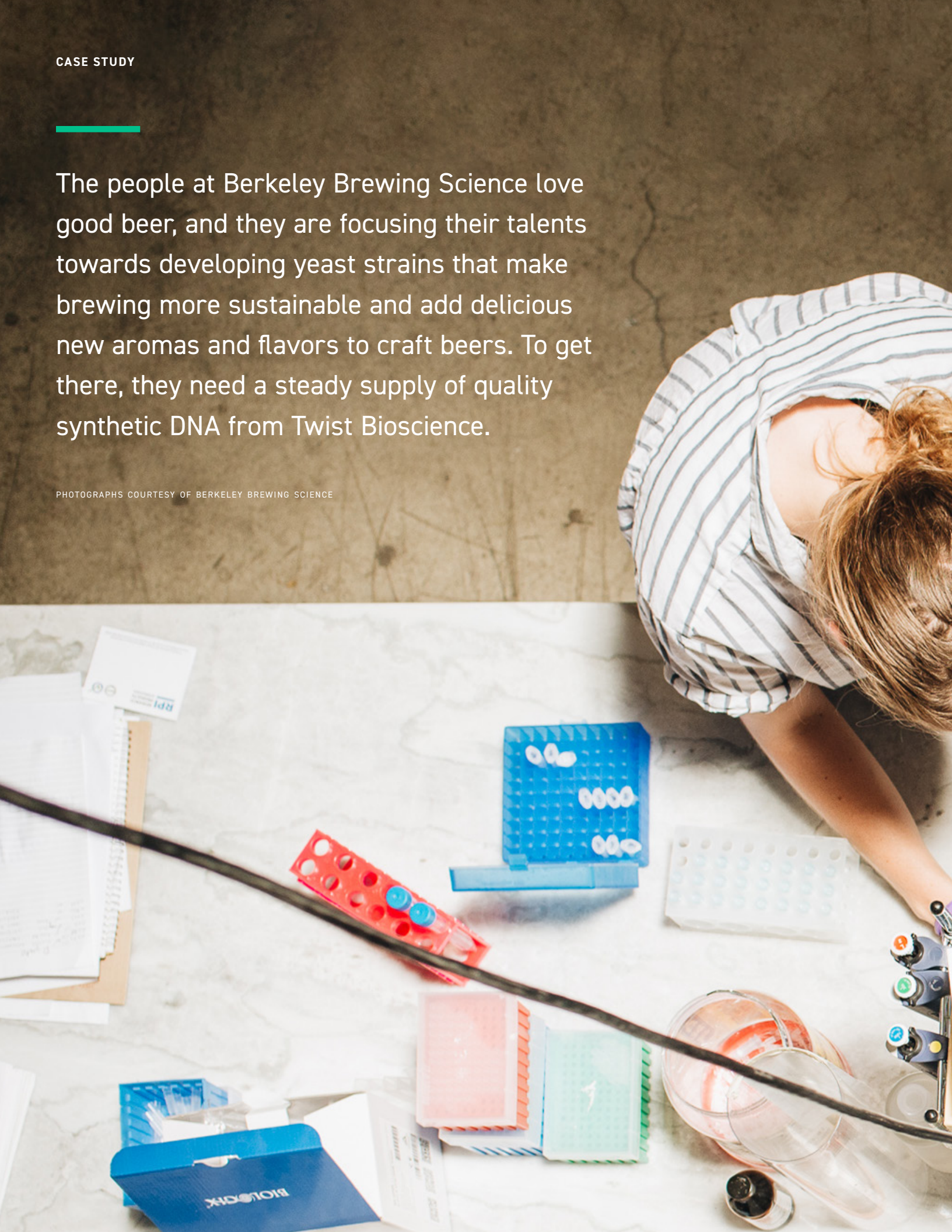
Twist Bioscience synthetic DNA helps Berkeley Brewing Science produce unique yeast strains for better brews

NOVEMBER 2019

CASE STUDY

The people at Berkeley Brewing Science love good beer, and they are focusing their talents towards developing yeast strains that make brewing more sustainable and add delicious new aromas and flavors to craft beers. To get there, they need a steady supply of quality synthetic DNA from Twist Bioscience.

PHOTOGRAPHS COURTESY OF BERKELEY BREWING SCIENCE




SARSTEDT
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EMMA

Beer has just a few simple ingredients: grain, hops, water and yeast. Like any science project, the quality of the end product depends a lot on these inputs.

There are more than 7,000 craft breweries in the United States, and that generates a lot of competition to develop unique beers. But with so few ingredients, there aren't many ways to add or subtract unique characteristics. On top of that, beer making is environmentally intensive: Growing the barley and hops to make just one gallon of beer requires as much as 590 gallons of water. Said another way, it takes 20 gallons of water to produce a single pint of beer. Using yeast to enhance the flavor profile also has the potential to improve the sustainability of brewing beer.

Quite possibly the first domesticated microorganism, brewer's yeast (*Saccharomyces cerevisiae*) plays an essential role in beer making. *S. cerevisiae* does a lot of the heavy lifting, converting sugar into ethyl alcohol and carbon dioxide. There is no fermentation without it.

Yeast and bacteria have been evolving new flavors for eons—consider bread, chocolate and cheese, all of which gain their flavor profile through these organisms. Berkeley Brewing Science (BBS) seeks to accelerate the process of flavor enhancement, adding flavors nature has already invented.

Because it's relatively easy to manipulate, brewer's yeast offers tremendous opportunities to enhance sustainability and add natural flavors to beer. Companies have gone to the ends of the Earth to capture novel yeast strains that will impart unique flavor profiles into beer. But those explorations are expensive and don't always translate into better brews.

BBS is taking a different approach. Rather than looking for yeasts, and hoping they might find useful traits, they identify natural traits and use molecular biology expertise to bring these traits to yeast. As a result, beer makers can produce hoppy beers with fewer hops and fruity beers with less fruit. The end result is a more sustainable, differentiated product that tastes great.

This innovative approach requires a steady supply of high-quality synthetic DNA—high fidelity clonal genes and gene fragments—which are provided by Twist Bioscience. These raw materials produce an ideal cycle: better DNA, better yeast, better beer.

We are trying to make better yeast strains for brewing, with a focus on increasing the sustainability of the brewing process. Growing and transporting hops uses a tremendous amount of natural resources. Our big idea is to make hop flavors from yeast in order to reduce the agriculture inputs that require lots of water and energy.

DR. RACHEL LI, BBS CO-FOUNDER

The BBS Origin Story

BBS started in Jay Keasling's UC Berkeley lab. Keasling runs the Joint BioEnergy Institute, which engineers microbes to produce biofuels. Charles Denby and Rachel Li, two BBS co-founders working in the lab, were avid homebrewers. In perusing the brewing science literature, they noticed that certain molecules called terpenes, which the Keasling Lab is well-known for producing in engineered microbes, are responsible for the delicious flavors in hops. However, hops are a natural resource-intensive crop, and reducing the amount of hop material required for brewing would reduce the water and energy needed to produce beer, making the brewing process more sustainable.

Traditionally, hops are cross-bred to create new varietals, then cultivated over a period of years or even decades to achieve a singular new flavor. In 2018, Denby and Li were co-first authors on a *Nature Communications* paper that showed they could bioengineer yeast to produce hoppy flavors in beer. This newfound ability provides an innovation engine for brewers, as they don't have to wait a decade or more for new hop varietals to be bred and cultivated.

Engineering yeast can also help the hop and beer industries survive increasing threats from climate change. Drought-resistant hop strains often do not produce the citrus and tropical fruit flavors many beer consumers enjoy. BBS yeast can fill that gap.

To start, the BBS team began experimenting with yeasts that produce the floral, citrusy flavors usually found in Cascade hops. Rather than taking ten years to produce a new hop varietal, BBS can develop a yeast strain in two to three months. Following that initial success, the company expanded its palette, producing yeasts that add a variety of flavors and aromas to beer.

BBS has several commercially-available strains, producing flavors and aromas that cross the spectrum from tropical fruit to citrus and floral to earthy. They also provide custom yeast strains tailored to a client's unique specifications. Synthetic genes give BBS the raw materials to create novel flavors and nose profiles that might otherwise be impossible, or extremely difficult, to make. BBS yeast is now being used by more than 30 breweries in the U.S., including some of the biggest names in craft beer.

Adding a Flavor

Brewers often add complexity to a beer's aroma and flavor by adding fruit flavoring agents. These compounds are often created through chemical synthesis or by extracting material from plants using solvents, neither of which is environmentally sustainable.

BBS solves this problem by integrating synthesized genes into pathway plasmids. These pathways are then transferred into an ale yeast strain commonly used by craft breweries. Once the genes are successfully integrated, the engineered strains are screened for production of desired flavor molecules. Ultimately, five strains with a range of concentrations are selected for test brewing.

The biosynthesis of flavor molecules is often mediated by large enzymes. Until now, the large size of many genes (sometimes larger than 3 kb) has discouraged BBS from having them synthesized, but Twist's gene-making capabilities have helped them overcome this barrier.

We think yeast-driven flavors are the final frontier in the beer industry. Working with our partners, we believe we are going to generate hundreds of new beer recipes that will be loved by existing beer drinkers and draw in new beer lovers while making the industry more sustainable.

MICHAEL MEIER, HEAD BREWER

The Right Raw Materials

Just as brewers need the best raw materials to make fine beer, BBS needs quality DNA to engineer their yeast. Equally important, DNA—whether in gene fragments or clonal genes—need to fit well into the BBS workflow.

BBS starts by identifying desirable traits and assess how different plant or yeast proteins can supply them. From there, they can order several gene variants and screen them to determine which ones are functional in brewer's yeast.

BBS can trust the fidelity of Twist's DNA, which is delivered in the vector of their choice and can be put directly into yeast. This streamlined process allows BBS to immediately start producing useful data.

In addition to short DNA fragments, BBS also receives long, clonal genes, which can encode for large or even multiple proteins, adding additional depth and dimension to the flavors in beer.

Better, More Sustainable Beer

Engineering new brewers' yeasts to create flavors and aromas gives brewers unlimited capacity to innovate new recipes and scale them on demand, all while making the brewing process more sustainable.

Thanks to the partnership between BBS and Twist, the future looks delicious! ■


On Tap
1) Control
2) Y20
3) G+
4) G+ Strata
5) High Sierra

WHAT CAN TWIST DO FOR YOU?

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