Plant 'blood' needs FDA OK

Impossible Foods submitted a petition to the US Food and Drug Administration in November to approve the soy leghemoglobin in its plant-based Impossible Burger as a color additive. Curiously, the burger has been served up in restaurants in the US since 2016, after receiving a Generally Recognized as Safe designation in 2014 by the same regulatory agency. But as the company gears up for a new use—to sell uncooked product directly to individuals in markets—the substance, which gives the meatless burger its red, bloody appearance as well as its meaty flavor, must undergo regulatory review under the 1938 Federal Food, Drug, and Cosmetic Act. The agency has tightened its scrutiny on colorings following debacles like the red dye #2 scare of the 1970's.

Impossible Foods, founded by Stanford's Pat Brown in 2011, makes animal-free hamburgers that look, taste and even bleed like the real thing. The key ingredient is leghemoglobin, a heme-containing plant analog of the oxygen-carrying animal protein hemoglobin; it is found in nitrogen-fixing root nodules of leguminous plants. Impossible Burgers, once found only in a few specialty restaurants, are now available in thousands of restaurants across the US and recently launched in Hong Kong; they even have halal and kosher certification.

Also soon on the menu is so-called 'clean meat' made from cultured animal cells (*Nat. Biotechnol.* **37**, 9, 2018). Closest to market may be JUST, founded by social entrepreneur Joshua Tetrick in 2011. The company seemed poised to launch its product in late 2018, although that hasn't happened yet. In the meantime, it has joined with Japanese meat and seafood suppliers to develop non-animal-derived products for their market. Such cooperation among suppliers is not happening in the US, where meat producers are hostile to this new breed of product.

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system to the point that it could be used in commercial seed production.

If, or when, that happens, an engineered apomixis strategy will fundamentally alter agriculture—most notably breeding and hybrid seed production. Breeders produce seed for hybrid crops, such as maize and rice, by crossing two genetically distinct parent lines. This gives rise to the toughest, highest yielding (and most expensive) varieties around. Seed producers can only generate such hybrids in fields with male and female inbred lines that are carefully developed. Companies keep the genetics of those lines secret—a business model that serves as the backbone of the seed industry (*Nat. Biotechnol.* **32**, 607–608, 2014).

The new apomixis technology changes that. Once a seed developer gets a good hybrid, the plant could be engineered to asexually produce seeds that are genetically identical to itself, eliminating the need for further two-parent crossing for that particular line of seed. That reduces the cost of production, and the savings can be passed on to the farmer.

That's a particularly big deal in developing regions and for smallholder farmers who can't afford hybrid seeds and are stuck planting inferior lines. Switching to hybrid rice could increase yield for many farmers by 20%, depending on the grower's location and crop management skills, Ali says.

Seed companies could also use the technology to turn traditionally nonhybrid crops, such as soybeans, into hybrids. "There is no simple, efficient, economical means of hybrid seed production for soybean or wheat," says Todd Jones, director of crop genome engineering at Corteva. As a result, companies typically sell inbred varieties of those crops, which may not be as vigorous as a hybrid version. Reducing the production costs of hybrid production with a clonal seed trait could make hybrid soybeans a reality. "That's where this [technology] would have a big impact," says Jones.

Of course, the technology could backfire on companies. Farmers could save their seeds, plant them, and get genetically identical plants the next season—undermining the seed industry's business model. But Jones says he doesn't see the new technology as a threat. If farmers save seeds instead of buying new ones each season, they would be missing out on new traits and genetics, which seed companies improve each year. "In fact, I think most seed companies see apomixis as another possible tool in the old toolbox, particularly with potential for plant breeding applications," says Jones.

And when it comes to seed saving, the seed industry has some advantages. "Seed companies have generated a couple of techniques to dry seeds properly, to coat them with fungicides and antimicrobial substances so they get a very high germination rate—nearly 100%—and this is something that the typical farmer cannot guarantee," says Dresselhaus. Plus, in countries such as the US where there are strong intellectual property laws and seed technology agreements, seed-saving growers would be breaking the law.

As transformational as the new tool is, Sundaresan stumbled on it by accident. His initial research goal had nothing to do with the seed business. "Apomixis wasn't actually on our radar. What we wanted to do was understand how a fertilized egg cell turns into a zygote" because of its implications for stem cells, he says.

His discovery builds on years of breakthroughs and incremental advancements made by many other researchers, who continue to pursue the apomixis trait. Peggy Ozias-Akins, a molecular geneticist at the University of Georgia in Tifton, for example, is credited with characterizing the role of *BABYBOOM* genes in apomixis in the grass *Pennisetum* (*Proc. Natl Acad. Sci. USA* **112**, 11205–11206, 2015). And Grossniklaus and colleagues have reported at several conferences since 2017 that they have engineered maize to asexually produce a small percentage of clonal seeds, using the gene *Nrf4* (non-reduction in female-4). A paper has not yet been published.

Industry researchers also have contributed resources to the apomixis cause. Che and other researchers at Corteva are part of a collaborative project called Capturing Heterosis, led by CSIRO (the Commonwealth Scientific and Industrial Research Organization) in Canberra, Australia, which aims to develop techniques to enable cowpea and sorghum plants to reproduce asexually. The project is funded by the Bill & Melinda Gates Foundation.

Wang, in China, says he hopes to license his method to more than one company. He is testing the technique in other crops, such as sorghum. But Sundaresan says he'll likely transfer the technology out of his lab. "We'll probably get back to understanding how egg cells turn into zygotes," he says. □

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