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t tastes like chicken." That's a common review of UPSIDE Foods' new trial product. Perhaps that's not surprising: it is, after all, chicken – at the cellular level. But the fillets are not from a slaughterhouse. They are grown in bioreactors in an urban factory in California.

A little over a decade ago, only a handful of researchers were investigating the potential of laboratory-made meat. The world's first cultured beef burger, which reportedly cost US\$325,000, was made by Maastricht University biomedical engineer Mark Post, who ate it at a press conference in 2013. Such products are now much closer to market: more than 150 companies around the world are working on cultured meat (from ground beef to steaks, chicken, pork and fish), milk or related 'cellular agriculture' products, including leather.

This June, US regulators passed lab-grown meat, making the country only the second in the world to move this food to market. Two companies, UPSIDE Foods in Berkeley and GOOD Meat (owned by Eat Just in Alameda, California), now have the green light to sell their cultivated chicken (since 2020, small quantities of GOOD Meat's chicken have been available for purchase only in Singapore). Observers expect at least one product to be available at a US restaurant this year, even if initially sold at a loss. Production plants are being built, and investment has hit \$2.78 billion, according to an industry report.

As commercial activity ramps up, academics in diverse areas, including food science and medical biotechnology, are improving cell culture and refining other parts of the process. The Good Food Institute (GFI), a non-profit organization based in Washington DC that was founded in 2016 to promote alternatives to animal products, has handed out \$17 million through more than 100 research grants to beef up the science on all aspects of meat alternatives; just over half the money went to cultivated meat. In 2021, Tufts University in Medford, Massachusetts, set up a Center for Cellular Agriculture, where around two dozen researchers now work on aspects from making to marketing cell-cultivated meat. And this April, the United Kingdom funded a Cellular Agriculture Manufacturing Hub led by the University of Bath.

Advocates say that cultured meat will slim the negative impacts of humanity's voracious appetite for flesh. Rearing livestock uses vast amounts of land and accounts for about 15% of global greenhouse-gas emissions. Consumption of red and processed meat has been linked to heart disease, diabetes and cancer; chicken farms can spread viruses such as avian influenza and promote antibiotic resistance; fish farms can pollute ocean waters. Globally, 80 billion animals die for our dinners each year – and a joint report by the United Nations and the Organisation for Economic Co-operation and Development predicts that global demand for meat will rise by 15% by 2031, thanks to a growing affluent population.

In response, the food industry is developing a bevy of alternative protein sources, from algae to insects (see page 26). But if the sensual experience of meat is a priority, then cell-cultivated meat might take top prize. "I've spoken to people who have been vegan for 15 years and they still crave meat," says Post. If meat-loving habits prove too hard to shift, he says, the obvious solution is to replace meat with meat.

Industry observers disagree, however, about how much cultured meat can be produced, how cheaply and whether the effort is worth it.

"There's such obvious benefits in terms of land use and biodiversity-related impacts. It's just a more efficient way to produce meat," says Pelle Sinke, an industrial ecologist at the nonprofit consultancy CE Delft in the Netherlands, who has worked on reviews^{1,2} of the carbon footprint and cost of cultured meat. But, he adds, there are still big questions about energy use, technology development and the market. Current versions are hundreds to tens of thousands of times more expensive than conventional meat¹. And to replace, say, 10% of the roughly



300 million tonnes of standard meat eaten globally each year could require construction of hundreds of thousands of bioreactors.

"I'm very critical of cultured meat," says Marco Springmann, a food-systems researcher at the London School of Hygiene & Tropical Medicine, who contributed to a 2019 World Economic Forum white paper on alternative proteins³ and the 2019 EAT Lancet Commission report on healthy, sustainable diets⁴. "I think it's a bad idea for health, for food security, and at the moment, also for the environment."

A better burger

The general recipe for cultured meat is to take a biopsy from an animal, nurture the cells in a nutrient bath so they multiply, coax them to differentiate into mature muscle or fat, and perhaps exercise the muscle cells and get them to bind into fibres. Some products, including one of GOOD Meat's offerings, combine animal cells with plant materials to make for a meaty-tasting nugget. Others, such as those from Aleph Farms in Rehovot, Israel, more ambitiously aim to make complex structures, including steak.

The main scientific and engineering challenges in the cultured-meat industry are largely the same as they were a decade ago: finding the best starter cells, mixing up a good 'feed' to help them grow and finessing the logistics of manufacturing.

Front of mind in all of these is cost. "Some people like to use the idea, 'oh, it's just like brewing beer'. But it's nothing like brewing beer," says biotechnologist Paul Wood at Monash University in Melbourne, Australia, who is critical of the industry. It is much harder and thus more expensive to nurture animal cells than microbes, he says.

In a report prepared for the GFI¹, Sinke and his colleagues at CE Delft laid out various projections for cultured-meat manufacturing. The most optimistic scenario speculated that production costs could, in theory, be beaten down to around \$6 per kilogram; their benchmark for conventional meat was \$2 per kg. Other studies are less hopeful: in one 2021 analysis using different assumptions, the lowest imagined cost of cultured meat production in future facilities was \$37 per kg⁵, a figure that would "likely preclude the affordability of their products as food", the study author concluded.

In search of the best, most efficient product, companies and researchers are tweaking each part of the meat-growing process.

They are using a wide variety of starter cells that can grow at different speeds or densities, and produce different textures or nutritional profiles. Post's company, Mosa Meat in Maastricht, the Netherlands, takes muscle stem cells from cow biopsies (trialling different animals and parts of the cow's body) and grows them into mature muscle fibres. These cells, however, can divide only around 30-50 times before they halt. Although a single biopsy could, in principle, provide hundreds of thousands of kilograms of meat, this method would still require frequent fresh supplies. Regenerative biologist Ori Bar-Nur at the Swiss Federal Institute of Technology in Zurich received a GFI grant to investigate how a cocktail of small molecules can get muscle stem cells to proliferate and differentiate into mature muscle simultaneously. This trick should make more muscle fibres, and larger ones, more quickly and cheaply than other methods.

Another option is to use 'immortal' cell lines, which could theoretically feed the world from a single biopsy. These can be made either through genetic modification – a route that faces a hefty regulatory burden in Europe – or by stumbling on spontaneous lines (as happened with the famous HeLa human cells and various research cell lines from mice and quail).

Israeli firm Believer Meats (formerly Future Meat Technologies) in Rehovot has published a study on its spontaneously immortal chicken fibroblast cells⁶. Fibroblasts, a type of connective-tissue cell that Wood calls "the weeds of

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GOOD Meat's cell-cultivated chicken is one of two products passed for US sale last month.

the cell-culture world", are fast and easy to grow – and can be converted to fat-like cells. The study produced cells at very high density – which should fit more biomass into a bioreactor and reduce costs if the system can be scaled up. Believer Meats is aiming high: it has broken ground on a facility aiming to produce 10,000 tonnes of cultured meat per year – orders of magnitude more than the tens of tonnes at other cultured-meat factories.

Some researchers say that the safety of consuming immortal cells, which could rack up mutations that might lead to tumours in the meat⁷, hasn't been fully established. But a March report by the Food and Agriculture Organization (FAO) of the UN on the safety of cultured meat concluded that the likelihood of such cells surviving packaging, cooking and digestion, and conferring any harm, "is not consistent with current scientific understanding"⁸.

To catalyse research on cultured meat, the GFI has compiled a catalogue of known useful cell lines (52 so far, from animals from cow to quail), and has partnered with the reagent company Kerafast in Boston, Massachusetts, to store and sell frozen samples of four cell lines so far. The catalogue contains several fish species, such as Atlantic mackerel (*Scomber scombrus*). GFI biologist Elliot Swartz notes that fish aren't typically hosted in university agricultural departments – but fish cells seem to be easier to cultivate because they are more tolerant than mammalian cells of low oxygen levels, a wide pH range and low temperatures.

By far the most expensive part of the process is the 'feed' required by the cells – a soup of amino acids, proteins called growth factors, sugars, salts and vitamins. The classic feed for cell lines in the lab is based on a cattle-blood derivative called fetal bovine serum, but that likewise comes with animal-welfare and sustainability issues. Replacing it has proved relatively simple, says Post. He and others have published about alternatives, and every company has a proprietary mix, he notes.

But the cost is still extremely high. Current commercial supplies of specific growth factors can cost millions of dollars per gram, says Post, because they are a niche product made to pharmaceutical standards in small quantities. However, research is starting to turn up some cheaper, plant-based alternatives⁹. UPSIDE Foods announced that it had made a serum-free feed in 2021, but the company says its initial products still use some animal serum.

Meanwhile, the logistics of the process hold plenty of opportunities for improvement. For example, food scientist Amy Rowat at the University of California, Los Angeles, received a GFI grant to develop edible beads as scaffolds for muscle cells to adhere to and flex against, to improve fibre texture. Other researchers are working out how to get cell cultures to flourish in ever-bigger bioreactors while feeding them with oxygen, pumping out their waste and avoiding damage to their structure.

Health kick

The aim of most companies, says Swartz, is to produce products that are nutritionally equivalent to or better than conventional meat. But many of the detrimental health issues of red meat will persist, notes Springmann. "It's very unlikely that this will be much healthier, if healthier at all," he says. Processed animal– plant hybrids such as chicken nuggets made of plants melded with chicken fat – expected to be the cheapest type of cultured meat product – could contain artificial colours or additives that give some consumers pause. The FAO notes that, as for other foods, cultured meat will need to be subject to limits on harmful bacteria, allergens, left-over antibiotics, growth hormones and other factors.

In terms of environmental health, culturing meat will use less land and water than producing beef, pork or chicken. But energy use is a serious issue – even assuming ambitious energy-use targets, by 2030 manufacturing cultured meat will still take about 60% more energy per kilogram than will beef production, the current worst offender. If that energy comes from renewable sources, however, the carbon footprint of cultured meat could be smaller than that of conventional meat, according to Sinke's analysis². A report by the University of Oxford, UK, finds that emissions per kilogram of cultured-meat protein could be smaller even than those from plant and insect protein¹⁰.

The first products to inch into the market have been chicken, even though – from a climate perspective – standard chicken has the smallest carbon footprint of the major meats. But Swartz notes that displacing chicken has real benefits for animal welfare, can limit zoonotic diseases and, by using less antibiotics, could stem the problem of antibiotic resistance¹¹. Most companies have plans to extend their range to beef and other meats.

Will anyone eat it? Surveys have found wide variability in the willingness of consumers to eat cultured meat – in part depending on what it is called. Attitudes are more positive towards 'cultured meat' and 'clean meat' than to descriptions using 'lab-grown' or 'artificial'¹². Some see a mass market beckoning in China, where meat consumption is rising particularly fast³.

In the Western world, cultured meat might, ironically, find a big market among vegetarians, notes Springmann. UPSIDE Foods, for example, has partnered with three-star Michelin chef Dominique Crenn, who plans to sell its product in her currently pescatarian restaurant.

If cultured meat is to make a dent in global problems, says Sinke, "it needs to replace conventional meat – not become another luxury item".

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