Cell-cultured meat: lessons from GMO adoption and resistance

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Abstract

This article discusses the choices and strategies that can hasten or delay the adoption of novel food technologies. We start by examining how genetically-modified food became an object of controversy in the United States and Europe. Then, we present lessons suggested by the history of GMOs for cell-cultured meat adoption. The history of GMOs suggests at least eleven concrete lessons for cultured meat adoption that remain under-discussed in the literature. This paper's findings diverge in several ways from received wisdom on cultured meat adoption. We argue, among other things, that genetic engineering firms understood their work to be humanitarian and environmentally-friendly and so were unprepared for popular backlash, that technology adoption is more readily affected by consumer activism when buyers in a supply chain exert more pressure on sellers than the reverse, and that focusing on the positive aspects of a technology is more successful for encouraging its adoption than responding to negative perceptions.

Introduction

The minute they tell you not to worry about something, you worry.

- London woman on GMOs, 1996¹

Efforts to produce animal products from cell cultures or genetically-engineered microbes like yeast rather than directly from animals' bodies have become more salient and successful since 2013, when Mark Post unveiled the first cell-cultured hamburger to wary journalists. Since then, a number of startups and industry observers have promised that cell-cultured meat is likely to reduce carbon emissions, reduce the land and water used for food, reduce or eliminate farmed animal suffering, and eventually outcompete conventional animal products with respect to cost. Evaluating the likelihood of these and other scenarios remains difficult, in part because no one knows how the development of cell-cultured meat will proceed and to what degree it will be adopted by consumers, food processors, distributors, and retailers. One underexplored way of evaluating different adoption scenarios for cultured meat is to examine how the rollout of other novel food technologies has transpired. For this reason, this article examines the adoption of and resistance to genetically-modified organisms (GMOs) in food as they unfolded in the US and Europe. We find that the history of GMOs offers a number of lessons for predicting the future of cultured meat.

¹ Quoted in Charles, 2001.

The early GMO and cell-cultured meat industries share a number of important similarities and dissimilarities. This article discusses these points of resemblance and difference in order to understand potential problems with the rollout of cultured meat. We are especially interested in questions around consumer perception, anti-technology activism, and the choices and strategies that can hasten or delay the adoption of novel food technologies. We begin by examining how genetically-modified (GM) food became an object of controversy in the United States and Europe. We examine five points of historical comparison between GMOs and cultured meat. Then, we present lessons suggested by the history of GMOs for cell-cultured meat adoption. The history of GMOs suggests at least eleven concrete lessons for cultured meat adoption that remain under-discussed in the literature. Our findings diverge in several ways from mainstream views of cultured meat (for examples of such views, see later discussion as well as Chiles, 2013; Gupta, 2018; Dutkiewicz, 2019). We argue, among other things, that genetic engineering firms understood their work to be humanitarian and environmentally-friendly and so were unprepared for popular backlash, that technology adoption is more readily affected by consumer activism when buyers in a supply chain can exert more pressure on sellers than the reverse, and that focusing on the positive aspects of a technology is more successful for encouraging its adoption than responding to negative perceptions.

Although cell-cultured meat has no clear predecessor product, GMOs make an unusually promising case study for cultured meat adoption. GMOs and cultured meat both began not with large multinational corporations but with small biotechnology startups (GMOs in the 1970s, cultured meat in the 2010s) that drew staff and techniques from academic biology and medical labs. GMOs share obvious consumer-facing similarities with cultured meat: because both are understood as technological changes that go into what humans eat, they face similar (often identical) consumer fears about safety, contamination, and unnaturalness. "Frankenfood," for example, has been used to describe both. This means that consumer attitudes and reception hold outsize power over both product categories in similar ways and for similar reasons. Beyond these family resemblances, however, GMOs and cultured meat also share a less obvious but no less important point: the industry structure of and decisions made by early genetic engineering firms closely map the current structure and choices facing cultured meat firms. Early GMO firms experienced similar financial pressure to raise money from investors to fund research into products that worked at demonstration scale in company laboratories but had not yet been brought down in price or up in production volume. They faced the constant threat of running out of financial "runway" before successfully scaling products. These factors induced GMO firms to make a variety of decisions about funding sources, mergers, product rollouts, regulatory avoidance or acceptance, and scaling that most cultured meat firms are just beginning to consider. Some of the decisions by GMO firms were effective and some were disastrous. Examining these choices allows for a more accurate vision of what to expect in the adoption of novel food technology generally and in cultured meat specifically.

We focus on GMO adoption in the US and Europe because that is where GMOs were developed, where they were first subject to public scrutiny, and where the terms of debate for GMO adoption first took hold. Europe and the US are also where the first cultured meat products were developed, where most (although not all) cultured meat startups are based, and the markets that are most targeted by current cultured meat firms (although not to the exclusion of countries like Singapore and China). For these reasons, GMO adoption in Europe and the US is likely to offer closer analogies to cultured meat adoption than other areas. This article is not intended to function as a review of cultured meat acceptance, but instead as a contribution that incorporates a historical comparative perspective that has so far seen little use. We think such comparisons, even when examining subjects with substantial differences, have proved useful in other areas.²

² See, for example, Anderson (2011), who compares animal rights and children's rights and makes a valuable contribution to the literature despite significant differences between the two groups and their legal status.

1 A brief history of GMOs and their analogies and disanalogies with cell-cultured meat

Contemporary genetic engineering began in 1972 when biochemist Paul Berg opened a loop of simian virus DNA, inserted genes from Enterobacteria phage λ , and reclosed the monkey virus's dimer circle with part of the lambda phage's DNA inside (Jackson et al., 1972). In 1973, Herbert Boyer and Stanley Cohen spliced a variety of genes into *E. coli*, including genes that endowed the altered bacteria with certain types of antibiotic resistance and genes from the toad *Xenopus laevis* (Morrow et al., 1974).

Safety concerns accompanied recombinant DNA research from the beginning. Paul Berg had originally intended to re-insert his hybrid DNA into *E. coli*, but refrained from doing so due to fears that the altered form of *E. coli* might spread to humans. In 1975, Berg organized the Asilomar Conference on Recombinant DNA, a meeting of about 140 scientists, lawyers, and doctors that put forward voluntary but influential guidelines on rDNA research, including steps like building containment procedures into experimental design (Berg, 1975).

By 1976, Boyer started Genentech, widely recognized as the first genetic engineering (GE) company, with venture capital funding. By 1977, the firm had inserted genes for insulin production into *E. coli* (Goeddel et al., 1979). Five years later, the FDA approved Humulin, a form of synthetic insulin pioneered by Genentech. Today, GM strains of yeast or *E. coli* produce most of the world's insulin, making insulin more widely available for diabetics (Aggarwal, 2012). Research into transgenic food began in the 1970s and by 1982 had produced the first transgenic plant, a tobacco plant resistant to the antibiotic kanamycin (Fraley et al., 1983). GM crops were commercialized in 1992, when Chinese farmers planted virus-resistant tobaccos (Clive, 1997). GM tobacco was pulled from China between 1995 and 1997 after buyers, especially US cigarette manufacturers, worried that consumers would reject GM ingredients.

The first commercially-available GM food, Calgene's Flavr Savr tomato, incorporated a gene that slowed pectin degradation and therefore extended the tomato's shelf life. Calgene introduced the tomato in May of 1994. Despite resistance from anti-GMO activists, the Flavr Savr remained in demand. Calgene identified the tomatoes as GM, using "label[s] on the cellophane wrapper on the tomato" and distributing "point of purchase brochures explaining how the tomato was genetically engineered" (Winerip, 2013). The tomato packaging displayed a phone number inviting customers to call with questions:

THANK YOU FOR BUYING MACGREGOR'S® TOMATOES. We Know You'll Enjoy Them.

Ne expend a lot of care and effort to give you delicious tomatoes with summertime taste all year After tasting MacGregor's Tomatoes, we know you'll think it's all worth it.

For more information about MacGregor's Tomatoes grown from Flavr Savr seeds, call 1-800-34TOMATO (1-800-348-6628), or write us at: Calgene Fresh, Inc. 1033 University Place, Suite 450 Evanston, Illinois 60201 Fig. 1. Flavr Savr packaging in the mid-1990s. See Michael Winerip, "You Call That a Tomato?" New York Times, June 24, 2013, <u>http://www.nytimes.com/2013/06/24/booming/you-call-that-a-tomato.html</u>.

However, Calgene, which had never been in the business of fruit distribution, struggled to lower production costs. The company made a number of simple errors, like destroying shipments by failing to pack trucks correctly. "Uh, we had to get a lot of the fruit out by shovel," Bill Hiatt, former VP of Research and Development at Calgene, admitted to the New York Times in 2013. Flavr Savr tomatoes never became profitable and Monsanto purchased Calgene on May 21, 1997.

As of 2016, twenty-six countries actively plant GM crops. The US, with 39% of global GM planting by area, leads the world. Brazil (27%), Argentina (13%), Canada (6%), and India (6%) follow (ISAAA, 2017). The US adoption of GM food varies significantly by crop. GM wheat, rice, potatoes, melons, and tomatoes all remain unplanted in the United States, despite successful tests, even brief commercialization. Most of these retreats came about as some variant of situations in which, as in the case of the GM potato, "foodservice chains told farmers they worried about campaigns portraying their french fries as made of GMOs" (Herring and Paarlberg, 2016).

Resistance to GE technology had existed from before the 1975 Asilomar Conference, and early activists like Jeremy Rifkin had criticized GMOs in the 1970s, but these concerns failed to show up in wider public opinion polling and consumption patterns until the late 1990s. As of 1995, public acceptance in the US for GMOs remained as high as 73% (Hoban, 1997).³ Support in Europe was lower, but much higher than it would be by 1999. Most early victories (prior to 1996) for US anti-GMO activists did not involve widespread public outcry, but came in the form of pressuring specific links in food supply chains (particularly foodservice firms) (Schurman & Munro, 2010). As a result of caution on the part of retailers and suppliers, products for direct human consumption were much more likely to be dropped than products intended for processing or animal consumption. Ron Herring (2016) writes that "[i]ngredients such as soybean oil, corn starch, or corn syrup derived from the processing of GE feed crops are pervasively used by America's processed and packaged food industries, but GE staple food crops, fruits, and vegetables intended for direct human consumption remain largely unplanted, even in the United States."

Despite early resistance, experts in biotech remained convinced through the mid-1990s that GM crops were poised for rapid uptake and adoption. The enthusiasm of firms, investors, and researchers "was infectious. Large corporations and finance... poured money into these new ventures and built a massive scientific-cum-business infrastructure dedicated to generating new discoveries and new products with recombinant DNA" (Schurman & Munro, 2010). In the late 1990s, GM crops were widely planted for the first time, raising their status as a public health concern. The late-1990s increase in GM planting was extremely rapid, especially in the US: global hectares planted with GM crops increased from 1.7 to 39.9 million hectares from 1996 to 1999, one of the fastest initial global adoption rates of a technology on record. As Adam Sheingate documents, rapid GMO uptake in the US was initially helped not just by a more accepting public, but also by a softer regulatory approach and different institutional handling of agricultural biotechnology compared to Europe and compared to medical biotechnology (Sheingate, 2006 & 2009).

By 1999, public opinion on GMOs in both Europe and the United States had soured. Nearly every EU country saw GMO opposition rise from 1996 to 1999, most by double digits (Bernauer 2016). France went from 46% opposed to 65%, Greece from 51% to 81%, Britain from 33% to 51%. (For context, this is comparable to the rate at which support for same-sex marriage increased in US General Social Survey data from 2010 to 2014 [AP-NORC, 2015].) It is worth noting that, though European public opinion moved in the same direction, levels of opposition in each country started

³ Percentage of respondents saying they would buy GM produce designed to resist insect damage.

from sharply different baselines and remained, even after increasing, quite different (see Costa-Font et al., 2006, for a discussion of the heterogeneity of European public opinion on biotechnology). Public opinion polling in the US showed lower overall opposition than in Europe, but also a modest rise, between zero and eight percentage points, from 1995 to 2000. For example, the number of US consumers reporting that they would be less likely to purchase foods modified for insect resistance increased from 23% in 1997 to 27% in 1999 [IFIC 1997, 1999].⁴

Gaskell (1999) shows that a greater increase in European press coverage of GM food from 1993 to 1996 preceded the greater rise in negative attitudes toward GM food among the European public. Interestingly, he does not find a correlation between negative sentiment and negative coverage (European news sources were not reliably more negative than US sources in the time period studied), but between negative sentiment and coverage itself. Gaskell argues that "in technological controversies it is the sheer quantity of press coverage that is decisive: The greater the coverage, the more negative the public perceptions."

Today, GMOs are widely grown in the United States, Brazil, and Argentina. However, they are not as widely planted or consumed as most experts in the 1990s thought they would be. Only one GM crop, a strain of Bt corn, can be legally cultivated in Europe. Spanish farmers grow it in modest quantities (in the 100,000-hectare range). In general, the EU has remained closed to GMO deployment.

Several analogies between GMOs and cultured meat emerge from this uneven history. First, GMO development began not with large multinationals but with small biotech startups in the mid-1970s. Though by the 1990s GMOs became synonymous with large agritech firms like Monsanto, to the extent that many contemporary writers and activists view GMOs as a product of these large corporations, they were first developed, and in several cases first commercialized, by a small group of startups that have more in common with present-day cultured meat startups than with Monsanto, Dow, or Tyson. Second, early attitudes around the technology (including those of experts and researchers) were extremely optimistic. The five years following the first demonstrations of viability (about 1973-78 for GMOs and 2013-18 for cultured meat) were characterized by a flurry of writing from experts inside and outside genetic engineering that GM food would alleviate world hunger, create a more sustainable food supply, and create healthier, cheaper food for consumers. Although the outlook for cultured meat is being steadily complicated (mostly by academics who are less widely read than stories touting cultured meat), its early reception closely resembles, sometimes verging on word-for-word repetition, that of GM food. Third, control of intellectual property mattered a great deal in the development and commercialization of GMOs. Because producing a new GM product depended upon specific techniques and knowledge, much of it novel and proprietary, firms were concerned to defend their methods and discoveries. Cultured meat firms, whose products are similarly research-intensive and depend upon proprietary knowledge, share similar concerns for similar reasons. Fourth, concerns about unnaturalness played a central role in the reception of GMOs. Activists portraved GMOs as different in kind from other foods, arguing that genetic engineering rendered GM food dangerous to consumers and the environment. The term "Frankenfood" crossed into the mainstream as an epithet for GMOs and since been applied to cultured meat. Fifth, the adoption or rejection of GMOs often turned on changes in framing and perception rather than shifts in technological, economic, or agricultural realities. For example, a shift in French discourse on GMOs in the late 1990s came about when, as Christophe Bonneuil et al. (2008) note, "'risk framing' successfully challenged... 'innovation framing'." That is, GMOs came to be discussed in terms of risks to health and the environment rather than in terms of their status as an interesting and useful innovation. The importance of framing is exacerbated by the fact that non-experts open made

⁴ Question text: "All things being equal, how likely would you be to buy a variety of produce, like tomatoes or potatoes, if it had been modified by biotechnology to be protected from insect damage and required fewer pesticide applications? Would you be very likely, somewhat likely, not too likely, or not at all likely to buy these items?"

decisions about GMOs on the basis of acceptability rather than risk (Slovic, 1987; Kolodinsky, 2018), so the difference between understanding GMOs as environmentally-friendly innovation and understanding GMOs as an unnatural result of corporate greed was more relevant than a sedulous accounting of risks and benefits.

Two apparent disanalogies are as instructive as the foregoing analogies. The first is that perceptions of secrecy and arrogance on the part of GMO manufacturers hurt GMO acceptance. This is often understood as something that cultured meat firms are unlikely to suffer from. This is not so, however, because, as will be discussed further in following sections, GMOs and cultured meat are not different in this respect. They are simply at different points in their respective lifecycles. Cultured meat is not associated with large corporations for the simple reason that large firms have not yet bought out the startups developing cultured meat. This historical fact, however, is correctable. The second disanalogy is that GMOs came to be, by the mid-1990s, aligned with certain incumbent agribusiness interests, and faced opposition rooted in a skeptical public. Cultured meat, on the other hand, currently faces opposition driven by established business interests (mostly ranchers). To a degree, as will be discussed in later sections, this is a difference in maturity between the two products, but it also reinforces a lesson about the determinative effect framing can have on a product. GMOs, after all, were once understood the way cultured meat largely is today: as a transformative technology that will contribute to a fairer, more sustainable food supply. Understanding how GMOs molted into an emblem of corporate overreach and what this can teach us about the pitfalls that await cultured meat remains one of the central tasks of the next section.

2 Points of comparison between GMOs and cultured meat

The similarities and differences between different technology adoption histories dictate the extent to which we can use one to understand another. We discuss five points of comparison between GM food and cultured meat: incumbent interests, each technology's roots in small startups, early predictions about the technology's potential, the importance of framing and perceptions of artificiality and naturalness, and corporate secrecy. While this discussion is by no means exhaustive, the extent of similarities between GMOs and cultured meat suggests comparisons between the adoption paths of the two can yield some understanding in the otherwise murky field of technological predictions (Fye, 2013).

We begin with an apparent disanalogy between GMOs and cultured meat adoption. In the case of GMOs, a majority of opposition came from consumer groups and environmental activists. Cultured meat, on the other hand, has mostly faced opposition (thus far) from competing producers like cattle ranchers' associations. Public opinion polls show fluctuating consumer reticence around cultured meat, with 76.4% of US respondents saving they would consider purchasing cultured meat in some studies (Bryant et al., 2019) and 33% in others (MSU, 2018; see Bryant & Barnett, 2018, for a systematic review of consumer acceptance of cultured meat). Because cultured meat is not well-known and because responses remain extremely sensitive to question phrasing, these numbers probably bears more resemblance to similar opinion research about other early technologies like self-driving vehicles, which shows similarly inconsistent numbers (Brenan, 2018; Hyatt, 2019). Because neither technology exists in any kind of robust, consumer-accessible form at this point. It is still too early to tell if consumer reticence around cultured meat bears more resemblance to early skittishness around GMOs or to early skepticism about, say, color television. Reasons that consumer reaction to cultured meat is likely to resemble that of GMOs include the fact that both are edible products and therefore involve certain concerns about what a person puts in their body, both involve concerns about naturalness and artificiality, consumers link both with health, and some of the same groups who oppose GMOs have made early criticisms of cultured meat (Catts & Zurr, 2013; Dilworth 2015; Willis, 2019). Whether or not consumer groups organize against cultured meat the way they have against GMOs, it remains that GMOs appear to have been

compatible with incumbent producers and retailers whereas cultured meat appears to threaten incumbent producers like ranchers.

However, there are reasons to think that this disanalogy is not as clear as it might seem. GMOs did face opposition from and were seen as incompatible with a variety of incumbent interests. For example, certain farms opposed GMO planting in the US and EU; some farmers, typically organic, who produced non-GMO product insisted on buffer zones and measures to avoid even the appearance of contamination; handlers and distributors found that having to separate GM product from non-GM product required expensive overhauls of their systems and squeezed margins; union interests remained ambiguous or opposed in many cases, notably in France (Schurman & Munro, 2010; Charles, 2001). In this respect GMOs' reception from incumbent interests was probably not substantially smoother than cultured meat's has been so far.

Our second point brings forward an important similarity: in the mid-1970s, GMO development began not with multinational corporations but with small biotech startups. Most of these startups had, like those working on cultured meat today, emerged from academic labs, as with Herbert Boyer's Genentech, the first genetic engineering firm of its kind. The GE sector grew rapidly. By 1982, over 100 biotech startups had been established (Schurman & Munro, 2010). The industry gradually underwent consolidation and a series of acquisitions. Eventually, a few large firms would come to control the development of GMOs. Cultured meat technology has certainly passed into a phase characterized by rapid growth in the number of startups working to bring products to market. It is unclear if this industry will undergo a similar rounds of consolidation and absorption by larger firms, although cultured meat investments by Tyson and Cargill reinforce the possibility.

Note that virtually all early GM firms eventually dissolved or were absorbed by larger firms. Most early biotech firms, even those that made technical contributions or were first to market with a novel product, did not grow into large or lasting companies. Recounting a history resonant for cultured meat startups, Schurman and Munro (2010) write that while "it was not difficult for a new company with a couple of distinguished scientists to interest some risk-oriented investors to support their endeavors for a couple of years," maintaining funding grew steadily more difficult. "What typically happened to firms," Schurman and Munro continue, "was that a large corporation would say, 'Well, you've really invented something, and we have money; we'll help you finish.' They made people an offer they couldn't refuse. For many start-up owners, being bought... by a bigger company or having one purchase a large equity share in the... firm was their best hope for staying in business." It is plausible that for-profit cultured meat ventures could encounter the same funding dynamics and incentives as genetic engineering firms did. This fact is important because acquisitions and investments by larger firms can affect the trajectory of an industry by changing business structures, the incentives of employees and companies, which endeavors are seen as worthy of research and development dollars, the cost-benefit ratios of different products, market access, scaling costs, and so on. For example, executives at acquiring companies like Novartis and DuPont "came from industries that were heavily dependent on intellectual property protection... so the need to have property rights over scientific discoveries was a standard element of their business strategies... competing for patent rights over genes... became a 'first principle' of the business" (Schurman & Munro, 2010). So, when smaller GE firms were absorbed by Novartis and DuPont, their intellectual property was taken up into a system of legal protection they may not have originally intended for it. Aggressive patenting, necessary or not, contributed to activist backlash and a souring of public opinion, particularly in Europe. "No Patents on Life" became one of the anti-GMO movement's most visible campaigns in the 1980s and 1990s. In Europe, the movement defeated an EU patent directive in an early blow against the biotech industry on the continent. Because the production of cultured meat involves specialized and novel techniques, intellectual property protection is likely to play a central role. If intellectual property decisions within cultured meat are framed as a "patents on life" issue or similar, this is likely to engender controversy.

Moreover, concentrating genetic engineering development in the hands of larger, older firms created liabilities in the form of negative public perceptions about the safety and acceptability of GM products. (See discussion of these liabilities later in this section.) Cultured meat development has not yet seen significant mergers and acquisitions, but it has seen investment from large firms like Cargill and Tyson. It's not yet clear if cultured meat will undergo a round of industry consolidation the way early genetic engineering did.

A third point of comparison: early predictions and goals for the technology were extremely optimistic, and this influenced the course of GMO development. Soon after the development of genetic engineering techniques in the 1970s, "the prospects for this... technology looked," to researchers and experts, "remarkably open and bright" (Schurman & Munro, 2010). Moreover, concerns about ecological and human wellbeing motivated much of the early research in genetic engineering, even at places like Monsanto. The early years of genetic engineering (starting in the early 1970s) are marked by predictions from those working on the technology that world-changing innovations would be delivered within five to ten years (Charles, 2001). Observers described a coming "gene revolution" that would "underpin a second Green Revolution" and "resolve" (not ameliorate, resolve!), among other things, "global hunger" itself (Schurman & Munro 2010). In a moment of excess, one researcher was quoted in the New York Times claiming to soon be able grow pork chops on trees (when he tried to get the statement changed, his boss told him it was "great publicity") (Charles, 2001).

GMOs' predicted potential and the stated motivations of researchers and businesses (to render the global food system safer and more sustainable) resemble the expectations and motivations currently animating research on and funding for cultured meat. In a 2015 interview, Mark Post, developer of the first cultured-meat hamburger, suggested that cultured meat could reduce the amount of land animals raised for food by 98%, from 1.5 billion to around 30,000 (Brannam, 2015). The Good Food Institute (2018) suggests that cultured meat adoption could restore agricultural land to "native prairie," thereby storing "up to 40 million metric tons of CO₂ in the soil each year," reduce deforestation, restore biodiversity, and sequester more carbon than it produces-and that's leaving aside claims about eliminating billions of years' worth of suffering produced by industrial animal farming. Though increasingly complicated by academic work (Galusky, 2014; Jönsson, 2016; Dilworth et al., 2015), highly optimistic predictions remain widespread among both lay and expert observers of cultured meat, evident at cellular agriculture conferences and mainstream press coverage alike. Jan Dutkiewicz (2019) documents how these conferences are filled with an investing parlance "of mainstream and scaling, the potential for triple-digit year-over-year growth and strategic synergies with incumbents in the food space." Unlike GM food, cultured meat has not matured to the point where predictions about its capabilities can be compared against real-world results, although analysis by Alexander et al. (2017), Lovvorn (2018), and Lynch & Pierrehumbert (2019) suggests that the holistic impact of cultured meat will almost certainly be more complex, and less rosy, than optimists predict.

Fourth, framing played a central role in which appeals to nature and concerns about artificiality were especially salient. The term "Frankenfood," first appearing in a 1992 letter to the editor of the New York Times (Federoff, 2004) and put to work by anti-GMO activists ever since, invokes the concerns about naturalness that animate the GMO (and now cultured meat) debate: that scientists' tinkering with nature has gone too far, that genetically-modified foods are stitched together from different organisms, that no one knows what the implications of such tinkering and stitching will be for human health and the environment, and that consumers are now expected to swallow it all. Sergio Dompe locates the genesis of GMO naturalness concerns in the fact that "the words 'genetic engineering' and 'biotechnology'... call up 'a glaring contradiction between life and technology, the natural and the artificial, that generates concern and apprehension.'" Dompe cites the switch from term "nuclear magnetic resonance" in hospitals to "magnetic resonance imaging," which reduced patient fears of radiation, even though radiation exposure from MRIs remained unchanged. "The moral of the story," he writes, is that "[i]nappropriate words, such as a

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misunderstood adjective or a bold juxtaposition, often influence our view of reality, feeding our suspicions and unspoken fears even where there is no justification" (quoted in Fedoroff, 2004). GM foods, as evidenced by their reception in Europe alone, were unable to leave behind naturalness concerns.

Cultured meat has, of course, attracted concerns that it is unnatural. Terms like "Frankenmeat" circulate widely, as does suspicion around cultured meat's artificiality (Fleming, 2017; ET Bureau, 2013). However, the history of GM food indicates that concerns about unnaturalness alone are not sufficient to provoke backlash (or else many medical procedures and drugs would go unused). The risk of backlash is highest, rather, when concerns from different areas overlap and intensify one another. In the case of GMOs, fears of corporate control of food intersected powerfully with fears about unnaturalness. Because cultured meat has attracted investment from large food conglomerates like Tyson and Cargill and could one day be produced and distributed by them, fears of corporate control are possible, even likely. Unnaturalness concerns are already present for cultured meat (Hopkins, 2015), of course, and so an intersection of these concerns that echoes the one that afflicted GMOs remains one of the most plausible scenarios for resistance to cultured meat.

More broadly, the adoption or rejection of GMOs often turned on changes in framing and perception rather than shifts in technological, economic, or agricultural realities. Christophe Bonneuil et al. (2008) argue that as the framing of the debate over GMOs changed in Europe, various "heroes and victims" were constructed by public discourse, which led to sudden shifts in priorities and, eventually, outcomes. Under different framing schemes, different issues were seen as salient. For example, under framing emphasizing "ecological risk,' the main victims were wild relatives of crops, and public-sector researchers carrying out biosafety research were heroic figures." When GM food was framed as a crop-contamination issue, "the main victims were organic farmers and others choosing not to grow GM crops." Moreover, framings like the "'right to information' and 'right to participation'" legalized and politicized the debate, emphasizing the failure of "local politicians... to adequately serve and protect their constituencies." A crucial, perhaps decisive, shift in French discourse on GMOs in the late 1990s came about when "'risk framing' successfully challenged... 'innovation framing'." A further example comes in Calgene's and Zeneca's marketing of their GM tomatoes and tomato paste as high quality because they had been genetically engineered, not in spite of it: Zeneca, for example, "cultivat[ed] British journalists and lin[ed] up partners in the food business. They'd already decided that [their] tomato paste would be packaged in special cans and labeled as the product of 'genetically altered tomatoes,' even though such labels weren't required.... They even turned genetic engineering into a marketing gimmick, advertising the launch of tomato paste as 'a world-first opportunity to taste the future.'" The experiment succeeded: "Through the summer of 1996 Zeneca's red cans of tomato paste, proudly labeled 'genetically altered,' outsold all competitors" (Charles, 2001). Calgene and Zeneca's examples reinforce the value of focusing on the positive aspects of a new product rather than endlessly rebutting fears and negative perceptions.⁵

Relevant industry actors seemed unready for how quickly framing shifts could happen and how consequential they could be. Cultured meat may be defined by "innovation framing," or something like it, for the moment, but the history of GMOs shows how quickly such a frame can be overcome or punctured by a new, fear-motivated frame.

Framing in public discourse is further complicated by that fact that non-experts often make decisions based on acceptability rather than risk. Gaskell et al. (2000) examine polling data from the US and Europe on GMOs and find that "[r]espondents with concerns about gene technology tended to think principally in terms of moral acceptability rather than risk—a significant difference from the way in which experts normally judge the acceptability of new

⁵ This dynamic famously played a role in the adoption of nuclear power: constant discussion of safety concerns, even if to answer them in a technically-sound manner, tends to replace positive frames of an issue with frames that center on whether a technology will cause cancer–even if there is little evidence that these concerns are warranted (Mohorčich, 2017).

technologies." A public motivated by moral acceptability is less likely to be swayed by arguments about the statistical safety of a new product like cultured meat and more likely to be influenced by arguments that emphasize the uncertainty associated with a product. This newness highlights the product's potential unacceptability. In this way and in ways previously discussed, how a new technology is framed can influence levels of adoption as readily as any underlying technical or economic change.

Fifth, perceptions of corporate secrecy and arrogance altered the course of GMO adoption, especially in Europe. High levels of competition between early biotech firms, the desire to control key intellectual property, and the race to bring products to market contributed to secrecy and aggressiveness within the industry. Observers of and participants in the early biotech industry describe a sense of urgency, even "adrenaline." As smaller biotech companies were absorbed, larger firms, Monsanto in particular, came under pressure to realize their large investments in biotechnology by producing lucrative new GM products. Genetic engineering projects were often chosen on the basis of potential market share and projected profits (Schurman & Munro, 2010). Moreover, shareholder value theory, ascendant in the 1980s, meant that executives were incentivized to generate short term profits rather than attend to environmental and social questions.

Monsanto, for example, refused to proceed slowly on introducing GM products to the European market. They "stormed" Europe, sending GM crops there unlabeled "despite being warned not to do so" (Schurman & Munro, 2010). This led to significant backlash on the continent. Simon Best, director of biotech projects at Zeneca at the time, tried to caution Monsanto CEO Robert Shapiro about the company's strategy in Europe, arguing that Monsanto was "severely underestimating the food situation in Europe. If you don't either label or start a communications program now, the food chain isn't going to back you up. And there's going to be a major consumer reaction. We haven't had enough time yet to get over the labeling issue. If you just ship these things in as a surprise, it's going to be a huge disaster." Shapiro told Best he was wrong. "Our people in Europe," Shapiro replied, "say that this is an exaggeration. We've talked to the right government people in all the countries of Europe." Reflecting on the exchange later, Best "thought Monsanto was behaving like a 'uniquely arrogant company'" that failed to "actually listen to the people who knew,... the food companies" (Charles, 2001).

In one sense, Shapiro wasn't wrong: Monsanto had talked to the right government officials in Europe and by March 1996 had gained regulatory approval for Roundup Ready soybeans. The problem was that European customers remained less trusting of government regulators than US customers, so regulatory approval counted for little among the European public. Revelations of deaths from BSE (mad cow disease) in the UK just five days after Roundup Ready's European approval did little to boost public confidence in regulators or food safety on the continent (Schurman & Munro, 2010). At the moment of its apparent triumph, Monsanto was barely two years away from a moratorium on GM crops in Europe.

It is tempting for cultured meat companies to shake their heads ruefully at the hubristic old days of biotech. Many cultured meat companies, it is true, understand themselves as more transparent, open, and conscious of consumer reaction than the large biotech firms discussed here (Chiles, 2013; Gupta, 2018). However, many biotech firms believed they were working toward a knowledge whose dividends would be widely shared: "These young genetic engineers did believe that their work would be good for the planet, possibly making it easier to grow food or reducing agriculture's dependence on chemicals. Some... working inside chemical companies... saw themselves as "green" revolutionaries fighting against the entrenched power of the chemists." These researchers saw chemical pesticides as part of "a dirty and regrettable past" from which "biology was the savior." Pam Marrone, a Monsanto engineer in the late 1980s, recounts then-CEO Dick Mahoney telling her, "Because of parathion [a hazardous insecticide], I don't ever want to be in chemicals again. And that's why we're in biotechnology" (Charles, 2001).

Moreover, if later interviews with researchers are to be believed, the working environment was, in general, far from toxic or cynical: "I had sworn I would never work in an industry," [Monsanto researcher Harry] Klee recalls. 'But when I got to Monsanto, it was just instantly apparent that if I wanted to do plant biotechnology, this was the place to be.'" Klee found Monsanto more collegial than academia: "In academia every colleague is also a competitor; every collaboration involves negotiation over credit. At Monsanto... much of that was stripped away. 'There was less ego involved'" (Charles, 2001). Charles, after interviewing scores of old genetic engineering researchers, argues that their "self-image [of helping the world] held a hazard. Those who occupy... the moral high ground are usually the least able to accept criticism or even comprehend it. When the genetic engineers found themselves attacked by a new generation of environmentalists, they were incredulous and hostile" (Charles, 2001). Those involved in cultured meat often talk about their work in similarly melioristic terms: one hardly needs to read past the headline of a 2018 article on Josh Tetrick, CEO of JUST, a plant-based and cultured meat company, to get the point: "JUST CEO Josh Tetrick created vegan mayo. Now, he wants to end world hunger" (Gupta, 2018).

It is important, too, to remember that genetic engineering was not always the province of large corporations. Shapiro (2018), differentiating GMOs from cellular agriculture products like cultured meat, writes that "GMOs are largely... produced by megacorporations like Dow AgroSciences and Monsanto, in part to maximize the output of feed crops for animal agriculture. Synthetic biology for agricultural products, on the other hand, is primarily being used by tiny start-ups seeking to solve key environmental problems by replacing traditional animal agriculture." This is true. However, many of the early genetic engineering firms were in fact tiny start-ups seeking to solve key environmental problems by replacing traditions of secrecy. Even as these firms grew, they remained open and transparent. Recall that Calgene and Zeneca advertised their tomatoes and tomato paste as genetically engineered products (Calgene in the US, Zeneca in the UK). Aggressiveness and secrecy became points of controversy only after older, larger firms came to dominate the production and distribution of GMOs. (Calgene was acquired by Monsanto in 1997 and Zeneca merged with Swedish pharmaceutical company Astra AB in 1999.) Present cultured meat companies may well be transparent, but it is unclear if firms will be able to remain so if and when they are taken into the larger food production system.

In the case of GMOs, cultural mismatches between companies and the markets they were selling to created additional liabilities. The European public (and some European food companies and regulators) largely saw Monsanto's attempts to introduce GMOs as evincing "arrogance, cultural insensitivity, and a deeply held belief that 'our way is better.'" Schurman and Munro (2010) argue that, in line with its "corporate culture," the firm "stormed" European markets, and in so doing committed "one cultural and political gaffe after another in its dealings with the European public and governments." In addition to shipping unlabeled GM soy to Europe (a choice that Zeneca's Simon Best had specifically warned Robert Shapiro against), Monsanto launched a tone-deaf advertising campaign in the UK in which it made claims, received as overblown and unsubstantiated, to the effect that GM crops would make possible "a tomorrow without hunger." These errors "made Monsanto into the perfect target for activists, enabling them to vilify the firm" and GMOs themselves (Schurman & Munro, 2010).

The furor in Europe poisoned Monsanto and genetic engineering's reputation beyond the continent. Outside of Europe and North America, "it is extremely difficult for politically cautious leaders in poor countries to be seen welcoming GM seeds if they are coming from a private corporate lab in the United States." A variety of governments treat GM crops with wariness rooted in skepticism of multinational corporations: "One reason," Robert Paarlberg testified before the US Congress in 2001, that "Kenya has not yet given final biosafety approval to the virus-resistant sweet potato is that the technology came originally from the Monsanto Company. One reason it has been hard in Brazil to get approval for RR Soybeans is that... this is a Monsanto product. One reason India has not yet given a final release to Bt cotton" is that it is made by Monsanto (Paarlberg, 2001). It is possible that smaller startups with more

transparent cultures are less susceptible to the dynamic that ensnared Monsanto. Indeed, early GE firms were not involved in the kind of controversies that led to GM crops' being shut out of Europe. However, there is no guarantee that invulnerability would persist if cultured meat were to undergo the consolidation and scaling that transformed genetic engineering firms.

3 Findings and recommendations

To recapitulate a central element of our argument, the history of gene editing commercialization can be broadly divided into two periods. The startup phase begins with the founding of Genentech in 1976 and extends into the mid-1990s. Its apex comes when Calgene and Zeneca bring GM tomatoes and tomato paste to market in 1994 and 1996. Optimism, external funding, rapid growth, and few commercial products characterize this period. The startup phase congeals into the second, corporate phase via investment and acquisition in the 1980s and 1990s. This phase is marked by larger, established firms like Dow Chemical and Monsanto bringing products to market and setting up profit structures around their intellectual property. Today's cultured meat (and plant-based meat) firms are not Monsantos with improved values: they are Calgenes and Zenecas, similar in company culture, values, funding needs, and facing the challenge of getting a profitable product to market without running out of funding. The industry structure of early biotechnology firms resembles the industry structure of early cultured meat research (small startups who are beginning to attract the notice of large, established firms). Moreover, the attitudes, vision, and stated aims of the researchers involved in biotechnology from the 1970s through the 1990s resemble those of cultured meat researchers and advocates today. The popular view that GMO controversies resulted from the involvement of large, corrupt "megacorporations" (Shapiro 2018) and that newer food technologies like cultured meat will avoid these controversies because they are being developed by smaller, socially-conscious startups is misguided. It is true that attitudes of secrecy and arrogance (or widespread perceptions thereof) by large GMO producers hurt the adoption of GM food. Monsanto's "storming" of European markets in the late 1990s proved especially damaging. This history should not reassure cultured meat advocates: rather, it indicates that cultured meat's trajectory will be radically altered if the industry undergoes a round of mergers and acquisitions similar to biotechnology in the 1990s. It is possible that larger firms could scale cultured meat products more effectively. It is also possible that the (real or perceived) corporatization of cultured meat production would provoke significant backlash, slowing or reversing adoption. In the case of GM food in Europe, the second factor probably outweighed the first. In the United States, the first factor probably outweighed the second.

In addition to this observation, the history of GMO adoption in the US and Europe suggests at least ten further lessons. The second takeaway is that much of the successful activist action against GM food came in the form of relatively small campaigns focused directly on companies (especially those occupying vulnerable positions in a supply chain). Comparatively less direct change came about via changing public opinion then using that broad base of support to alter policy. Focused campaigns, even if small, achieved more than broad changes in public opinion.

Third, unwillingness to regulate GMOs in a timely manner likely soured the public on GM food. As Sheingate (2006) documents, congressional hearings and regulatory activity around medical biotechnology were substantially more stringent and attentive to risks than they were about agricultural biotechnology. Moreover, "hearings on medical applications engaged a broader array of interest groups" than did those on agricultural biotechnology, "where commercial interests, such as those of industry, were often predominant" (Sheingate, 2006). Monsanto's head of regulatory affairs argued that Reagan-era anti-regulation FDA spokesman Henry Miller "did more harm to biotechnology than [anti-GMO activist] Jeremy Rifkin ever did" (Eichenwald, 2001). This suggests that targeted regulation can alleviate concerns and improve the odds of adoption.

Fourth, early experts on GE technology predicted a future in which applied genetic engineering had solved major problems in agriculture, nutrition, sustainability, and food security. Many of their evaluations match, contour for contour, current predictions around cultured meat. However, virtually none of the world-changing GMO predictions came to pass. Cultured meat researchers, even (or especially) those familiar with the technology, should be wary of any consensus view that claims that cultured meat will transform the global food system in this or that radical way.

Fifth, no GM utopias arose, but none of the apocalyptic predictions about GM food came true either. Many biotech researchers would respond that this was no surprise, because worries of apocalypse were ludicrous to begin with. Ludicrous or not, biotech companies should have taken opposition to GM food more seriously. Many of the most obvious blunders (e.g., Monsanto's strategic decisions in the second half of the 1990s) could have been avoided by taking activist concerns, public fears, and the cultural differences between markets seriously.

Sixth, the history of new technologies indicates that concerns around unnaturalness alone are not sufficient to provoke widespread backlash (or else many prescription drugs and medical interventions would go unused). The risk of backlash is highest, rather, when concerns from different areas overlap and intensify one another (e.g., corporate control of food meets unnaturalness). Concerns about unnaturalness are usually stronger for food than for other applications like medicine. However, this rule is not absolute: food technologies like pasteurization and the use of antibiotics on farmed animals have spread widely while some medical technologies like cloning and vaccines have provoked opposition.

Seventh, supply chain structure influenced the behavior of distributors and retailers. The wave of European supermarkets dropping GM ingredients in the late 1990s was made possible by highly competitive retail firms who wouldn't risk losing customers, by a supply chain structure in which sellers were susceptible to pressure from buyers, and by the failure of American biotechnology firms to secure buy-in from European processors, handlers, and retailers (Schurman, 2004; Schurman & Munro, 2010; Bernauer, 2016). Supply chain dynamics will affect cultured meat's rate and manner of adoption. Securing buy-in from retailers and other distributors has already been a matter of consequence for plant-based meat companies like Impossible Foods (whose partnership with the largest food distributor in the United States, Dot Foods, was crucial to its expansion) and Beyond Meat (whose products Whole Foods began carrying nationwide in April 2018). It is too early to tell if Impossible and Beyond products will resemble Calgene's Flavr Savr, a novel product from a young company that sold well and generated interest before being discontinued, or will become permanent, scalable components of the food supply.

Eighth, patenting and intellectual property protection pose backlash risks for cultured meat firms. Any move that could be interpreted as enforcing "patents on life" could be especially damaging to public opinion. Decisions by biotechnology companies, particularly Monsanto, to defend patents on, for example, Roundup Ready soybean seeds by suing farmers for replanting these seeds has contributed to the view that GMOs are at bottom a tool for agricultural firms to control the world's food supply (Kimbrell & Barker, 2013).

Ninth, the framing of an issue often overwhelms technical or economic facts, so paying attention to the way a new technology is being understood remains important even if the benefits of that technology seem obvious and the drawbacks inconsequential. Public discussion often has the effect of rendering benefits abstract and distant and dangers personal and close.

Tenth, focusing on the positive aspects of a technology has been more successful than publicly responding to negative perceptions. Zeneca and Calgene's marketing of their tomato products as genetically engineered and better for it succeeded in a way later public relations strategies around GM food did not. The examples of Zeneca and Calgene reinforce the value of focusing on the positive aspects of a new product rather than endlessly rebutting fears and

negative perceptions. The limits of a rebutting strategy became apparent in debates over the adoption of nuclear power in France, the US, and elsewhere (Mohorčich, 2017). Constant discussion of safety concerns, even if to answer them in a technically-sound manner, tends to replace positive frames of an issue with negative frames centered on safety. Non-experts often make decisions based on acceptability rather than risk, so a technical totting-up of the relative risks and benefits of a technology is likely to be subsumed to an acceptability/non-acceptability binary in public discourse.

Finally, living in countries that require GMO labeling is positively correlated with being critical of the technology (Bernauer, 2016). Various attempts to impose de facto labeling requirements on cultured meat have already been made by cattlemen's associations and lawmakers (Dutkiewicz, 2018; Siegner, 2019). Cultured meat manufacturers may proactively differentiate their products from slaughtered meat, sidestepping labeling concerns. Cultured meat companies have an interest in differentiating their products to, among other considerations, avoid the perception of sneaking into markets the way GMO producers tried to.

Conclusion

The present state of GMOs offers a vision of the future that represents, in our view, a realistic slow-adoption scenario for cultured meat two to three decades from now. Today, GMO adoption grows only incrementally. Most gains come from areas where GM crops are already widely planted. Research to develop new GM products continues more slowly and with fewer funds than if the market for GMOs were larger. Thomas Bernauer (2016) notes that the most substantial obstacles confronting GM food adoption today are "low consumer trust in the safety of the food supply in key markets" (especially in the EU), concerns about "long-term health and environmental effects," questions about corporate control of food supplies, and "insufficient consumer benefits from GE products." In short, altering genes seems risky, untrustworthy corporations are involved, and GM food doesn't seem any tastier or safer, in part because most agricultural GM applications have gone toward fractional cost decreases and yield increases, both of which are less apparent to consumers.

The history of cell-cultured meat remains unwritten. However, the history of GMO adoption in the US and Europe suggests that cultured meat adoption will be slower, harder, and more complicated than the technology's supporters predict. Cell-cultured meat will face challenges around, at a minimum, industry structure, safety, unnaturalness, funding, and intellectual property control. Studying the history of new food technologies promises to shed further light on the nature of these challenges.

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