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A call for an 'Asilomar' for cultivated meat and seafood

he idea of 'cultivating' meat is almost 100 years old. In December 1931, Winston Churchill famously wrote that "in 50 years we shall escape the absurdity of growing a whole chicken in order to eat the breast or wing by growing these parts separately under a suitable medium". His prediction was off by some 30 years but was nevertheless fulfilled as a proof-of-principle: in 2013, the world's first-ever cultivated hamburger was developed at the modest price of US \$325,000. The following decade brought several improvements in cell lines, culture media, bioreactors and scaffolds¹. Whether it will soon be possible to cultivate meat at market scale and in a cost-competitive manner remains debated^{2,3}. Nevertheless, the sizable market opportunity has led to considerable investment (in total, almost \$3 billion)⁴.

Ethical advantages aside, cultivated meat is predicted to have a lower environmental burden than that of conventional meat⁵, to limit the spread of antibiotic-resistant bacteria6 and to reduce the risk of zoonosis⁷. Collectively, the field is attracting the attention of governments and other entities that are looking for solutions to tackle these pressing issues of our time. In this context, a recently proposed bill by the Italian government to ban cultivated meat is not only anachronistic but also creates a dangerous precedent that could stifle this emerging sector elsewhere. As representatives of the field who are suffering the effects of this antagonistic political and social climate at first hand, we wish to contextualize and raise international attention on this matter and ultimately to propose a call for action to mitigate it and prevent similar developments elsewhere.

Cultivated meat is currently approved for sale only in Singapore, having been 'greenlighted' in December 2020 by the Singapore Food Agency. Nearly two years later on 10 November 2022, Coldiretti (a leading Italian farmer's association that is known for its conservative positions) launched a petition that proposed to ban the production, use and commercialization of 'synthetic food'⁸. The petition targeted cultivated meat in particular, affirming that 'it is produced by crazy cells grown in a bioreactor', 'it is dangerous to the environment, using more energy and generating more pollution', 'it is dangerous for human health' and 'it limits consumer freedom leading to homogeneous food choices' (translations by the authors). We have already debunked such misinformation elsewhere and will not discuss it here any further⁹.

The timing of the petition is interesting to consider, however. It was launched less than three weeks after the installment of the new conservative government of Prime Minister Giorgia Meloni, which had just rebranded the Italian Ministry of Agricultural, Food, and Forestry Policies by adding 'Food Sovereignty' to the title (MASAF). It also anticipated by three days the first FDA preapproval of a cultivated meat product in the USA¹⁰ – a coincidence that was capitalized upon as evidence of the pressing need for the petition. A second preapproval by the FDA of a similar product, approximately three months later¹¹, added fuel to the raging fire. The petition allegedly collected half a million signatures 12 – about 30% of Coldiretti affiliates and around 0.8% of the Italian population – and gained the support of several local and regional administrations. Ultimately, on 28 March 2023, it was formally embraced by the Italian MASAF and Ministry of Health, which proposed a joint bill draft that if approved would ban the production and commercialization of cultivated meat foods and feeds in Italy – a first in the world.

The proponents of the bill argue that it is justified by the 'precautionary principle', which is presented as the lack of evidence that cultivated meat is safe for human consumption. This is inconsistent with its actual definition in Regulation (EC) No. 178/2002, which states that the precautionary principle applies only to food that is being already commercialized in the EU should preliminary data suggest a potential hazard. To be commercialized in the EU, cultivated meat would first need to be evaluated by the European Food Safety Agency (EFSA) as a 'novel food' under Regulation (EU) 2015/228. So far, the EFSA has not even been asked to evaluate any cell-based food product¹². The second stated aim of the

bill is to 'protect the cultural heritage of Italy'. To achieve this, the bill aims to prevent the import of cultivated meat from abroad: such a law would violate Article 34 of the Treaty on the Functioning of the European Union, which prohibits quantitative restrictions to imports between member states.

This is not the first time that the Italian government has proposed prohibitionist bills that are not based on the available scientific evidence and are contradictory to current legislation. Unfortunately, some of these past initiatives ended up affecting many other countries, as in the emblematic case of genetically modified organisms (GMOs). With the decree of former Prime Minister Giuliano Amato in August 2000, the cultivation of GMO-derived edible products was forbidden in Italy on the basis of concerns about alleged soil contamination. A year later, Pecoraro Scanio – then Minister of Agricultural, Food and Forestry Policies – took a further step by banning open field trials of GMO crops, despite the fierce opposition of Italian scientists (such as Nobel Prize laureate Renato Dulbecco and Rita Levi Montalcini). Some 20 vears later. GMOs are still not cultivated in Italy but over 80% of animal feed is imported as GMOs¹³ – an economic paradox that compounds the scientific one. Unfortunately, this phenomenon spread across the rest of Europe and resulted in an 87% drop in GMO field trials by 2003 (ref. 14). Despite a 2006 World Trade Organization ruling that the EU's so-called de facto moratorium on GMOs was illegal, only a few European countries cultivate GMO crops today. For instance, only 1.5% of EU corn crops are GMO¹⁵. On the other hand, the EU imports approximately 60 million tonnes of GMO products annually, which are mainly used for animal feeding¹⁵.

This example of the long-lasting negative effect on scientific and societal progress of a misguided policy should be a clear warning sign to all who are witnessing the current social and political turmoil around cultivated meat in Italy. However, we should not be discouraged nor feel helpless. Rather, we should seek inspiration from positive examples from the past that could point us toward possible

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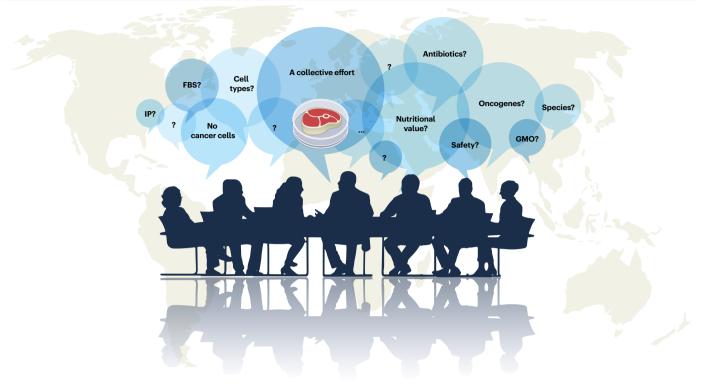


Fig. 1 | **An Asilomar for cultivated meat and seafood.** As biotechnologists who are experiencing the attempts of the Italian government to ban cultivated meat and seafood, we humbly call for action from all stakeholders: either we

self-regulate and build consensus on critical issues to reassure both the public and governments or history may repeat itself with prohibitions that could stifle this emerging field. Modified from an image designed by rawpixel.com/Freepik.

actions to counter the current situation and prevent it from escalating.

The development of recombinant DNA technology in the early 1970s was followed by a call for caution by its inventors, who urged colleagues worldwide to halt experimentation until the safety concerns about this powerful method could be assessed and addressed¹⁶. Discussions led to the 1975 Asilomar Conference, which involved over 100 scientists, lawyers and physicians and resulted in a set of shared guidelines for the safe use of recombinant DNA. These self-regulations provided the basis for the National Institutes of Health 'Guidelines for Research Involving Recombinant DNA Molecules', which enabled scientists to continue with their research and achieve fundamental biotechnological advances. Importantly, Asilomar also moved the scientific debate more into the public domain and increased the interest of the public in biomedical research. It is likely that had Asilomar not taken place, societal and political dynamics would have taken the decision on how to control recombinant DNA technology out of the hands of scientists, which could potentially have led to fear-driven bans or otherwise unreasonable regulations that could have stifled progress.

We propose that the cultivated meat and seafood field is at a crossroads, and needs an Asilomar moment to prevent the political and cultural debate on the topic that is currently shaking Italy from spreading to other countries where governments have held agnostic positions or from reversing progress that has been made in countries that have understood and supported this food (Fig. 1). Our recent experience defending the field from detractors in our country suggests that we may have mitigated the development of such an antagonistic social and political climate through earlier self-regulation and by involving the public in the scientific discourse. The lack of a consensus about what should and should not be done in the field has given detractors ample space to cherry-pick individual studies or products, which are then often misrepresented or taken out of context with the ultimate effect of scaring or outraging the public.

For instance, although it is widely agreed that fetal bovine serum (FBS) is essentially antithetical to the purpose of cultivated meat and should be avoided, the first commercialized cultured meat product is currently made using FBS – as are the two products that were preapproved by the FDA. Detractors have leveraged this as evidence that cultivated meat does not solve, but instead worsens, animal welfare. The question arises of whether we, as a field, should have preempted such misrepresentation by indicating to regulators that only products based on FBS-free media should be approved for commercialization.

Cell immortalization is another challenging topic. On the one hand, it is generally seen as necessary to support the large-scale expansion that is key to cultivating meat without relying excessively on animal biopsies. However, immortalization can be obtained through very different methods (ranging from the selection of spontaneous mutations to viral transduction to precise genome editing). The first method is very popular as it bypasses GMO regulations but is being leveraged by critics who argue that scientists are growing 'crazy' cells that are more akin to tumors than muscle. Viral transduction poses safety concerns that are well understood and could be mitigated but may be difficult to communicate

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and justify in the wake of the COVID-19 pandemic. Finally, the application of genome editing in cellular agriculture divides the field: some avoid it, owing to fear of public backlash and/or stringent GMO regulations (particularly in the EU). However, if properly communicated and regulated, genome editing could provide an invaluable way to reproducibly generate immortalized cell lines that maintain genomic stability. Still, we may wish to develop guidelines for which genetic modifications are acceptable: for instance, whether we should put overexpressing a species' own telomerase gene to bypass cellular senescence and knocking in an oncogene or knocking out a tumor suppressor to promote cell growth on the same level.

The choice of species for cultivated meat is also nontrivial. Besides the obvious taboo about culturing meat from human cells, several open questions exist. For instance, cultivating food and feed from animal models such as zebrafish or mice would be much more straightforward given the decades of relevant know-how¹⁷, but it is unknown whether this will be acceptable to the public and regulators. Another issue is whether we should mix cells or even genes from different species (as recently showcased by the development of a 'mammoth meatball' made of sheep myoblasts that carry a mammoth gene¹⁸): are marketing stunts worth facing the backlash to what detractors are already calling 'frankenfood'? We should also consider the potential dangers of expressing potential foreign allergens and whether nutritional enrichment of cultivated meat justifies species 'mix and match'.

The use of antibiotics in cellular agriculture is another divisive topic. Although it would be ideal to avoid their application completely, many are skeptical that this will be possible². Detractors leverage this division to suggest that cultivating meat needs more antibiotics than conventional animal agriculture; we should consider proposals for feasible middle-ground alternatives that ensure both product safety and protection from antibiotic resistance.

There are several other issues worth discussing, such as the standards that we should aim to achieve regarding safety, nutritional value and life cycle impact of the process. All of these have been questioned by detractors, as it is unclear where current prototypes and products stand on many of these issues. Notably, most of the research and development in the cultivated meat field has taken place in private ventures. Thus, it is important to consider how to build a knowledge-sharing framework that is compatible with market dynamics, but does not leave any one country behind (that is, through affordable intellectual property (IP) licensing). This would be key to debunking the dystopian scenarios that are evoked by detractors such as Coldiretti, which claimed in their petition that 'synthetic food is in the interest of a few who want to monopolize the supply of food in the world'.

All in all, we see a dire need for an international discussion board that involves not only scientists and industry representatives to tackle the key technical aspects, but also humanities scholars to convey essential input as to the social, legal and political ramifications of cellular agriculture. By generating a consensus around a set of shared guidelines for the field, we could enter a productive dialog with the public and the regulators and hopefully prevent reiterating blunders from the recent past.

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S. Bottini, C.F. and N.S. wrote the first draft of the manuscript. A.B., S. Biressi, L.C. and C.G. revised the manuscript. A.B. conceptualized the manuscript and coordinated the group. Equally contributing, and jointly supervising, authors are listed alphabetically in the author list.

Competing interests

A.B. is an inventor on a cellular agriculture patent and a cofounder, shareholder and member of the scientific advisory board of SoundEats, a cultivated seafood company. L.C. and S. Biressi are inventors on a provisional patent application on cellular agriculture. The remaining authors declare no competing interests.