

Novel foods in the European framework: benefits and risks

Monica Marilena Miazzi, Maria Dellino, Valentina Fanelli, Isabella Mascio, Domenica Nigro, Claudio De Giovanni & Cinzia Montemurro

To cite this article: Monica Marilena Miazzi, Maria Dellino, Valentina Fanelli, Isabella Mascio, Domenica Nigro, Claudio De Giovanni & Cinzia Montemurro (23 Dec 2024): Novel foods in the European framework: benefits and risks, *Critical Reviews in Food Science and Nutrition*, DOI: [10.1080/10408398.2024.2442062](https://doi.org/10.1080/10408398.2024.2442062)

To link to this article: <https://doi.org/10.1080/10408398.2024.2442062>



© 2024 The Author(s). Published with license by Taylor & Francis Group, LLC.



Published online: 23 Dec 2024.



Submit your article to this journal [↗](#)



View related articles [↗](#)



View Crossmark data [↗](#)

Novel foods in the European framework: benefits and risks

Monica Marilena Miazzi^a, Maria Dellino^a, Valentina Fanelli^a, Isabella Mascio^a, Domenica Nigro^a, Claudio De Giovanni^{a#} and Cinzia Montemurro^{a,b,c#}

^aDepartment of Soil, Plant and Food Sciences (DISSPA), University of Bari Aldo Moro, Italy; ^bSpin off Sinagri s.r.l, University of Bari Aldo Moro, Bari, Italy; ^cSupport Unit Bari, Institute for Sustainable Plant Protection, National Research Council of Italy (CNR), Bari, Italy

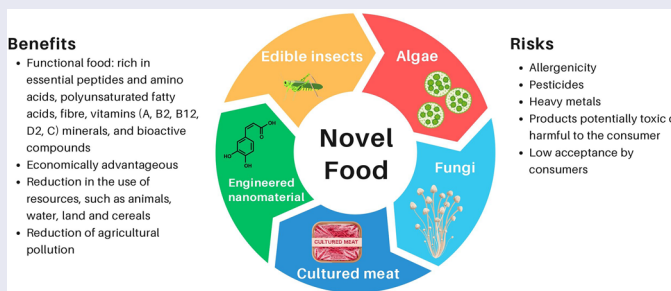
ABSTRACT

Given the rapidly increasing global demand for food, it is mandatory to consider new sources of nutrients, safe and sustainably produced protein foods to complement the current traditional and limited sources of protein in the human diet. In recent years, a wide range of nontraditional protein foods have been explored, prompting the European Union to legislate on how novel foods can be introduced and traded on the European market to ensure their safety. This review will illustrate the range of novel foods authorized in the EU and their potential impact on human health, highlighting the gaps, the potential risks, and the future research opportunities and perspectives.

KEYWORDS

Allergen detection; biotechnologies; functional foods; superfoods; biofortification

GRAPHICAL ABSTRACT



1. Introduction

The global population currently stands at 7.5 billion people and is expected to increase to 9–10 billion by 2050 (UN 2019), resulting in growing food demand by 70% and increasing pressure from food production systems on natural ecosystems. Fifty per cent of the Earth's habitable land is used for agricultural production (van Dijk et al. 2021), and food system chain, including production, storage, transport, processing, packaging, retail and food waste, is recognized to be responsible for more than a third of global gas emissions, particularly related to animal husbandry (Crippa et al. 2021). Reducing proteins of animal origin and replacing them with alternative protein sources is the cornerstone of future food security (Mazac et al. 2022; Bull et al. 2022), as this would reduce the overall impact by more than 80% without compromising nutrition (Parodi et al. 2018; Tzachor, Richards, and Holt 2021). One way to address this problem could be the use of foods that derive from sources other than traditional agriculture and livestock, such as insects, algae, fungi etc. that

are collectively defined as novel foods. Compared to animal-based meals, novel food has up to 88% less global warming potential, 83% less land use, 87% less scarcity-weighted water use, 95% less freshwater eutrophication and 78% less marine eutrophication, and 92% less impact on soil acidification, while providing the same nutritional value as vegan and omnivorous meals (Mazac, Järviö, and Tuomisto 2023).

In Europe, the Novel foods have been regulated since 1997 by EU Regulation 258/97, which defines them as foods or ingredients intended for human consumption that have never been consumed on a significant scale in Europe prior to the adoption of Regulation 258/97 (https://food.ec.europa.eu/system/files/en?file=2016-10/novel-food_guidance_human_consumption_en.pdf) and provides a detailed list of Novel foods constantly updated by the Commission Implementing Regulations (EU) (Truzzi et al. 2023). According to the law, they include “foods or ingredients with a new or intentionally modified primary molecular structure; foods or ingredients consisting of (or isolated from) animals, plants, micro-organisms, fungi, algae or jellyfish; foods produced from materials of

CONTACT Maria Dellino  maria.dellino@uniba.it

[#]Cinzia Montemurro and Claudio De Giovanni contributed equally to this work.
© 2024 The Author(s). Published with license by Taylor & Francis Group, LLC.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License (<http://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited, and is not altered, transformed, or built upon in any way. The terms on which this article has been published allow the posting of the Accepted Manuscript in a repository by the author(s) or with their consent.

mineral origin and products and food ingredients which have undergone a nonstandardized production process which gives rise to significant changes in the composition or structure or nutritional value or level of undesirable substances” (https://food.ec.europa.eu/safety/novel-food_en). The measure also applies to foods traditionally consumed outside the EU, in the category “traditional foods originated from a third Country”, provided they have been safely used in at least one non-European Country for 25 years. Regulation EU 2015/2283 replaces Regulation EC 258/97, simplifying and updating it to take account of changes in food consumption, habits, and technology. It updates the categories of novel foods to include nanotechnologies and foods of plant origin obtained by non-traditional breeding to improve their composition or structure significantly. These include foods made from micelles or liposomes, novel carbohydrates such as new dietary fibers, the oligosaccharides of milk identical to those found in humans (e.g., sucrose, lactose) and the new foods intended to replace sugars, as well as food supplements such as plant extracts, synthetic cannabidiol and, temporarily, cloned animals intended for food purposes. Products with specific legal requirements such as GMOs, enzymes, additives, flavorings, vitamins and minerals that do not result in molecular differences that require “novel food” status are excluded (by Article 2 of Novel Food Regulation (EU) 2015/2283).

In this review, we aim to provide an overview of the complex topic of novel foods and the benefits and potential risks associated with their use and marketing in Europe. This will contribute to a better understanding of the topic and the examination of possible associated problems and will contribute to a fruitful debate to better respond to the challenges that will arise in the field of nutrition in the future.

2. Novel foods marketed in Europe

2.1. Cultured meat from animal cells

Over the last five decades, the demand for meat has steadily increased so that animal proteins currently account for up to

40% of total protein consumption, and a similar increasing trend is predicted for the near future (Sans and Combris 2015). Against this background, cultured meat (CM) could be an effective alternative to mitigate the effects of intensive agriculture, resource consumption, agricultural pollution and ethical issues related to animal life (Stephens et al. 2018) by reducing gas emissions by up to 92% and land use by up to 90% (Zhang et al. 2021).

CM is a laboratory-grown meat obtained by the proliferation of muscle and fat cells in a suitable culture medium containing nutrients, hormones, and growth factors or, in some cases, fetal bovine serum (Post 2014). Changes in the composition of the culture medium and the use of scaffolds allow the immature cells to differentiate into skeletal muscle, fat and connective tissue, making up the meat that can be harvested, processed and packaged into final products. The entire process takes between 2 and 8 wks, depending on the type of meat cultured (Post 2014) (Figure 1).

CM could also help to reduce the problem of antibiotic resistance in livestock (McNamara and Bomkamp 2022), as the risks of contamination would be minimized in a strictly controlled cycle and the use of antibiotics would be limited to the pre-production phase (Ong et al. 2021; Saied et al. 2023). Finally, CM also offers the opportunity to produce stand-alone products with improved sensory and nutritional properties that are specifically tailored to a particular consumer with specific nutritional needs (Treich 2021).

Today, a growing number of companies are working on commercializing and scaling up cultured meat production. Cell-based foods are currently authorized in Singapore (from 2020) and the USA (from 2023), but not in Europe, although the first production of CM took place in 2013 at Maastricht University (Netherlands) using primary bovine skeletal muscle cells. Since then, several public and private laboratories have entered this field of research, making it a very tangible hypothesis for a new type of food (Stephens et al. 2018). Nevertheless, the EU is funding projects for CM as a promising contribution to achieving the goals of the European Green Deal objectives for fair, safe, healthy and

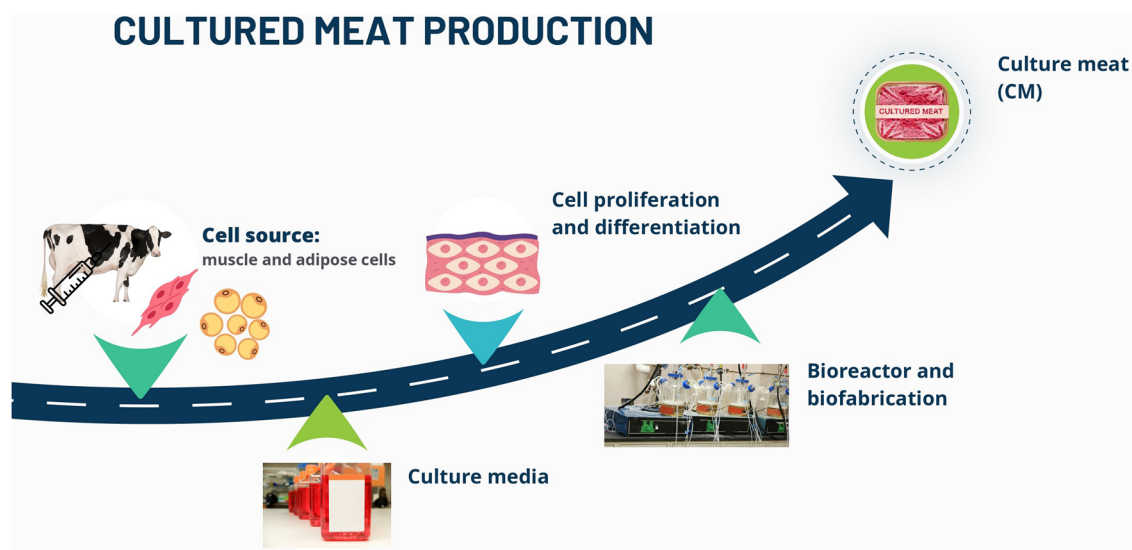


Figure 1. Schematic process to produce of cultured meat (CM).

environmentally friendly food systems (<https://www.horizon-europe.gouv.fr/cultured-meat-and-culture-d-seafood-state-play-and-future-prospects-eu-33346#:~:text=Cell%2Dbased%20agriculture%2C%20and%20especially,for%20fair%2C%20safe%2C%20healthy%20and>).

On the other hand, cultured meat, like genetically modified organisms, is not readily accepted by consumers and raises concerns about naturalness, food safety, religion, ethics and especially health risks (Mancini and Antonioli 2020). While it is generally agreed that the potential problems and allergenicity are the same as for conventionally produced foods (FAO and WHO 2023; Routray et al. 2016), there is particular concern that genetic material could be taken up by the gut microbiome or human intestinal cells and result in products that are potentially toxic or harmful to the consumer (Wang et al. 2019). The Food Standard Agency UK (<https://www.food.gov.uk/research/identification-of-hazards-in-meat-products-manufactured-from-cultured-animal-cells-glossary>) lists the hazards in meat products manufactured from cultured animal cells including: the risk of contamination from components used in the different cell culturing stages; the risk of exposure to antibiotics and fungicides residues used in the culturing; the safety of the bioreactor, pipes, pump etc used for cultures (Warner 2019); the biological risks associated with the components derived from animals such as the fetal bovine serum lines (Marga et al. 2017). Further studies are needed on these safety aspects of cell-based foods to improve stakeholders' ability to control them and consumers to acquire information for greater awareness (Ong et al. 2021).

2.2. Edible insects

The consumption of insects may be considered unusual in many Western cultures, but in many Asian, African and Latin American countries they are already part of the diet (Aidoo et al. 2023). More than 2000 species are consumed whole or used as ingredients in the preparation of traditional dishes, as they are an excellent source of protein and other valuable nutrients (Barennes, Phimmasane, and Rajaonarivo 2015; Oibiokpa et al. 2018). Insects contain essential long-chain, polyunsaturated omega-3 fatty acids such as α -linoleic acid and significant amounts of crude fiber, especially chitin from the exoskeleton (Mokaya et al. 2023). They are also a valuable source of peptides and essential amino acids which act as prebiotics in the human gut, as well as vitamins, minerals and 10 to 50% fat content depending on species, habitat, diet, reproductive stage, age and sex (Belluco et al. 2013). In Europe, insects are increasingly seen as a potential and cost-effective substitute for traditional animal protein and as an environmentally sound solution for a more sustainable diet, due to their high feed conversion efficiency, and reduced greenhouse gas emissions, use of water and arable land. However, while in Eastern countries many companies have already started to breed insects for food and feed on a commercial scale (Cadinu et al. 2020; Dobermann, Swift, and Field 2017), in Europe, they represent a very small niche market and only four insect species are currently authorized for human consumption by the European

Commission: *Tenebrio molitor* larva (yellow mealworm), *Locusta migratoria* (migratory locust) *Acheta domestica* (domestic cricket) and *Alphitobius diaperinus* (Ruggeri et al. 2023). On the other hand, the use of insects as food is also a cause for concern, as they can potentially trigger immunoglobulin-E (IgE)-mediated reactions that lead to allergic sensitization or clinical symptoms in already sensitized individuals (Precup et al. 2022; Ma et al. 2023). Allergenicity is not yet fully understood, and the literature is sparse and mainly refers to Asian and African populations (Ribeiro et al. 2018; Pali-Schöll et al. 2019; Taylor and Wang 2018). Insects produce several classes of allergenic proteins (Schlüter et al. 2017), of which tropomyosin (TM) is the most important and most extensively described. Tropomyosin is a protein involved in muscle contraction and exhibits high cross-reactivity due to the high amino acid sequence homology between variants (López-Pedrouso et al. 2023; Ma et al. 2023). The allergenic potential of insects depends on insect growth conditions, including diet, life-cycle stage and processing methods (e.g., boiling, frying, roasting) (Murefu et al. 2019; Ribeiro et al. 2021; Palmer et al. 2020; Imathiu 2020). This can be exploited to reduce the risk of allergy, but many other variables play a role in allergy, including individual sensitivity, so further studies on the allergenic proteins, their structure, post-translational modifications and interactions within the food matrix are needed (López-Pedrouso et al. 2023) to safely manage this aspect of insect-based foods.

2.3. Fungi

Five million species of fungal organisms are estimated to exist worldwide, including yeasts, molds, and fungi which grow in water, trees, soil and air, and contribute to degrading nearly all hydrocarbon wastes, releasing carbon, oxygen, nitrogen, and phosphorus into the soil and the atmosphere (Hawksworth and Lücking 2017; Niego et al. 2021). Fungal fruiting bodies, mycelia or extracts have been used directly as food or to produce various fermented foods for centuries (Tamang, Watanabe, and Holzapfel 2016) due to their high nutritional value and the attributed antimicrobial, antitumor and antioxidant properties (Duvnjak et al. 2016). They are rich in phytosterol derivatives such as ergosterol, sterol and β -d-glucan (Kalač 2009), which have a cholesterol-lowering effect (Cheung 2010, Wasser 2011), and a good source of iron, copper, riboflavin, niacin, and fiber and, release protein, vitamins B, C, and D, and selenium when cooked (Muszyńska et al. 2018).

Due to all these properties, fungi are increasingly being consumed in new forms on the European market, especially as food supplements under the Novel Food Regulation. In 2019, California-based mushroom manufacturer Monterey Mushrooms producer received authorization from EFSA to market *Agaricus bisporus* powder fortified in vitamin D following ultraviolet irradiation treatment (<https://www.efsa.europa.eu/en/efsajournal/pub/7326>). Similarly, "FermentIQ[™]" from MycoTechnology Inc, the high-protein (> 75%) dehydrated powder of peas and rice fermented by Shiitake mycelia (*Lentinula edodes*), received recognition as a novel food (Bisen et al. 2010) and is used for baked goods, beverages,

soups, meat, etc. (Cardwell et al. 2018; Clark et al. 2022). This product is valued for its nutritional components, which include free sugars such as arabinose, arabitol, mannose, mannitol, trehalose and glycerol; vitamins (B2, B12, D2) and fiber and various bioactive polysaccharides such as β -d-glucan, heteroglucan, xylomannan, eritadenin (Hobbs 2000) and lentinan, which has immunostimulant and immunomodulatory properties (Melgar-Lalanne, Hernández-Álvarez, and Salinas-Castro 2019). Another fungus authorized as a novel food in the EU in 2023 (by Golden Biotechnology Corp) is *Anthrodia camphorate* (syn: *A. cinnamomea* (niu-chang-chih)). This species, a parasite of the tree *Cinnamomum kanehirae* (Bull camphor tree) Hayata (*Lauraceae*), which grows in the forests of Taiwan at an altitude of 200–2000 m, is traditionally used in Chinese medicine (Geethangili and Tzeng 2011). It contains several active ingredients, including terpenoids, polysaccharides, ubiquinone derivatives (anthroquinonol), maleic and succinic acid derivatives, polyphenols, etc., which make it a beneficial supplement for food and beverages.

Although the use of fungi as food is growing, little is known about their allergenicity, which has been observed in 2.5–6% of the population after exposure and consumption (Pravettoni, Primavesi, and Piantanida 2014, Goikoetxea, Fernández-Benítez, and Sanz 2009). The growing role that they will play in the modern food industry makes it necessary to deepen the safety aspects of their use and increase knowledge of their interactions with immunological processes (Singh, Garg, and Upadhyay 2024).

2.4. Algae

According to the definition of the European Committee for Standardization (CEN 454), the term “algae” refers to a group of aquatic photosynthetic organisms that includes the eukaryotic pluricellular macroalgae and microalgae, as well as the procaryotic cyanobacteria (Leyland, Leu, and Boussiba 2017; Adl et al. 2019; De Araujo and Peteiro, 2021). Algae play an important ecological role by contributing to the regulation of marine ecosystems through photosynthesis and the production of organic food molecules and oxygen, thus ensuring the survival of marine species (Lafarga 2019). They have been consumed for centuries, but recent research on their properties has shown the possibility of expanding their use as food through new production methods (Choudhary, Chauhan, and Mishra 2021; Diaz et al. 2023). Different algae species grow relatively fast and are capable of producing 167 times more biomass per year than corn while using the same amount of land (Matos et al. 2017). Today, they contribute to almost 30% of global aquaculture production and provide food rich in fiber, micronutrients, bioactive compounds and proteins that benefit human health (Bonaccorsi et al. 2020), such as essential amino acids like glycine, arginine, glutamic acid and alanine (Aguilera-Morales et al. 2005). They also contain indigestible polysaccharides (dietary fiber), which improve gut function and provide polyunsaturated fatty acids for a balanced diet. They are rich in vitamins A and C, niacin and folic acid, as well as various pigments with antioxidant, antimicrobial, anti-cancer and anti-inflammatory

properties (Wells et al. 2017). Algae are also a source of iodine, an essential mineral that is important for the proper functioning of the thyroid gland (Healy et al. 2023). In Europe, the use of algae as food continues to grow in parallel with the European Commission’s actions to promote their sustainable production and use, to ensure their safe consumption, improve their use in the EU and promote consumer acceptance. Currently, there are 1550 different species of algae growing in EU waters, but only 23 have been included as foods or food supplements in the EU Novel Food Catalog (De Araújo and Peteiro 2021). Although algae are considered a safe food, their consumption in the human diet raises concerns about the contaminants that may be present in the growing environment, such as heavy metals. Banach, Hoek-Van Den Hil, and Van Der Fels-Klerx (2020) have identified four threats to the European algae chain associated with arsenic, cadmium, iodine and Salmonella. While hygienic problems can be solved by growing edible algae in unpolluted waters, the problem of allergenicity of algae in the population seems to be more complex, and few studies are available about the topic. Various proteinaceous allergens have been identified in algal foods (allergome.org), but some of these have not yet been biochemically characterized and require further investigation.

Several studies have identified potential allergens in algae, namely phlorotannins (Barbosa et al. 2018), polysaccharides (Borthakur et al. 2012) and proteins (Polikovskiy et al. 2019). These components are capable of triggering allergies to varying degrees. Whether these molecules trigger allergenicity in humans requires further investigation. Most studies have focussed on the unicellular species *Spirulina* (*Arthrospira*) and *Chlorella* (58%), which are widely used in the dietary supplement industry. Several studies using rodent models show that some algae-derived components such as carrageenan can induce intestinal inflammation and significantly alter the composition of the gastrointestinal microbiota (Benard et al. 2010; Chassaing et al. 2017). In addition, food supplements derived from *Spirulina spp.* and *Chlorella spp.* contained cadmium and mercury, probably due to the lack of quality controls (Rzymiski et al. 2015). Toxins were also found in dietary supplements derived from microalgae due to cross-contamination with toxin-producing cyanobacteria (Hadi and Brightwell 2021; Quintieri et al. 2023).

2.5. Nanoscience and nanotechnology

Nanotechnology deals with the use of nanoparticles that have an average size of one hundred nanometers (nm) or less in at least one dimension, to alter the chemical and physical properties of materials, often turning an ordinary unreactive material into a highly reactive substance (<https://www.fsai.ie/getattachment/b644eff2-1549-46ff-93da-3a309bed2d6d/nanotechnology-and-food.pdf?lang=en-IE&text=.pdf>). The use of nanomaterials in the food sector is regulated by Article 3(2)(f) of the Novel Food Regulation (EU) 2015/2283, as this technology is increasingly being applied to food to develop certain desired properties or to improve packaging. Nanotechnology is used in food to enhance taste, color,

Table 1. List of advantages and disadvantages in the main categories of novel foods.

Novel food	Reference EU	Advantages	Disadvantages	Ref.
Cultured meat	Regulation EU 2015/2283	<ul style="list-style-type: none"> • Efficient choice compared to conventional livestock systems; • Reduction in the use of resources, such as animals, water, land and cereals; • Reduction of agricultural pollution and eutrophication; • Reduction of food-borne illnesses; • Antibiotic-free meat; • Healthier meat consumption adapted to specific dietary needs. 	<ul style="list-style-type: none"> • Allergenicity, • Products potentially toxic or harmful to the consumer. 	Treich 2021; Ong et al. 2021; FAO and WHO 2023; Routray et al. 2016; Wang et al. 2019; Nawaz et al. 2019.
Edible insects	Regulation EU 2015/2283	<ul style="list-style-type: none"> • Functional food: rich in essential peptides and amino acids, long-chain omega-3 polyunsaturated fatty acids, fiber, vitamins and minerals; • Economically advantageous compared to animal and vegetable proteins as they require fewer resources. 	<ul style="list-style-type: none"> • Main allergenic proteins: tropomyosin, myosin, actin, troponin C, tubulin, hemocyanin, defensin, arginine kinase, triosephosphate isomerase, α-amylase, trypsin, phospholipase A, hyaluronidase. 	Alexander et al. 2017; Belluco et al. 2013; Schlüter et al. 2017; Ribeiro et al. 2018; Varunjikar et al. 2022; Hall, Fitches, and Smith 2021; Bose et al. 2021; Leni et al. 2020.
Fungi	Regulation EU 2015/2283	<ul style="list-style-type: none"> • Cholesterol-lowering effects; • Good source of iron, copper, riboflavin, niacin, and fiber and, release protein, vitamins B, C, and D, and selenium; • Immunostimulant and immunomodulatory properties. 		Cheung 2010; Wasser 2011; Muszyńska et al. 2018; Melgar-Lalanne, Hernández-Álvarez, and Salinas-Castro 2019
Algae	Regulation EU 2015/2283	<ul style="list-style-type: none"> • foods rich in fiber, micronutrients, bioactive compounds, essential amino acids (glycine, arginine, glutamic acid and alanine), vitamins (A and C), niacin and folic acid, pigments with antimicrobial, anticancer and anti-inflammatory properties; source of iodine 	<ul style="list-style-type: none"> • Presence of dangerous molecules for human health such as Arsenic, cadmium, iodine and Salmonella • Main allergenic proteins: C-phycoerythrin, Thioredoxins, Superoxide dismutase, Glyceraldehyde-3-phosphate, dehydrogenase, Triosephosphate isomerase, viz. calmodulin, Fructose-bisphosphate aldolase 	Bonaccorsi et al. 2020; Wells et al. 2017; Healy et al. 2023; Petrus et al. 2010; Bianco et al. 2022.
Nanotechnology	Regulation EU 2015/2283	<ul style="list-style-type: none"> • Foods products with certain properties and characteristics desired. 	<ul style="list-style-type: none"> • Probable nanotoxicity resulting from inhalation or dermal exposure. 	Allai et al. 2023

flavor, and texture or to increase nutritional value. Organic nanoparticles can be used to encapsulate nutrients to improve their bioavailability or to mask an undesirable taste or odor; inorganic nanoparticles, including gold, silver and titanium can be used as additives and preservatives. Nanomaterials can also be used in food packaging, for example to improve the flexibility or temperature and moisture stability of materials, or can release antimicrobial, antioxidants or flavoring compounds to improve the shelf life or sensory characteristics of the product. They can also contain nanosensors capable of identifying specific microbial or chemical contaminants and are therefore useful for food biosafety and traceability.

With the increasing use of these nanomaterials in food, concerns have arisen about their safety (He and Hwang 2016). Foods containing nano-ingredients or produced using nanotechnology are considered novel foods and must therefore undergo a safety assessment before being placed on the market, following the EFSA guidance on the risk assessment of the application of nanotechnologies in the food and feed chain (<https://doi.org/10.2903/j.efsa.2021.6768>). Moreover, engineered nanomaterials in food, including plastic layer materials that is not in direct contact with the food, must be correctly labeled on the list of food ingredients. Nevertheless, very little information is available on the biological effects of nanomaterials and their toxicity, and knowledge on the fate and interaction of nanoparticles that enter the human body through skin contact, inhalation or ingestion is limited. In particular, the use of inorganic nanomaterials such as silver and titanium, both

directly in food and in food contact materials, requires a rigorous safety assessment, and the immunomodulatory effect of nanomaterials in already sensitized individuals needs to be further investigated (Yoshioka et al. 2017).

3. Safety of novel foods

Legislative instruments for regulation and control of novel foods exist in the EU and non-EU countries, reflecting different approaches underlying food regulatory systems. Authorities in Canada, Japan, the United States and Australia are not particularly concerned about novel foods as long as they do not pose a risk to human health. In the United States in particular, the food industry has a high degree of freedom as long as the general legal requirements for food safety are met, even though manufacturers have a general responsibility. Australia and Canada have a regulatory system that is more similar to the European one, but with significant differences in the definition of what is covered by novel food legislation and the authorization procedures. Although explicit pre-market authorization is required in Australia and Canada before novel foods can be placed on the market, the differences in the concept of novel foods determines that many more foods can be placed on the market easily and quickly. On the contrary, the more cautious approach and a broader interpretation of the precautionary principle applied in the EU require that even foods that do not pose a risk to human health must be explicitly authorized before they can

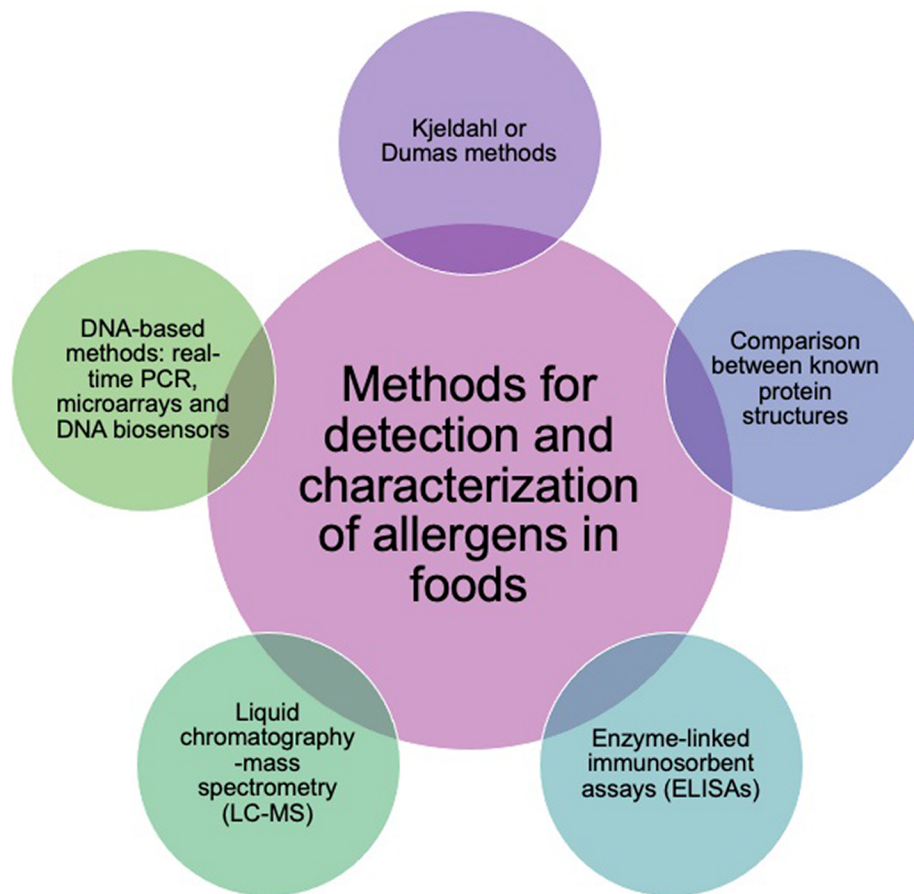


Figure 2. The most important methods for the detection and characterization of allergens in novel food.

be placed on the market if they are considered novel food. In Europe, the precautionary principle is expressed in the fact that companies producing innovative foods must obtain authorization before placing a product on the market and must fulfill the safety requirements of the European Food Safety Authority (EFSA), which are based on all available information, including primarily the results of toxicity studies and any adverse effects using human data.

The safety assessments are carried out at the request of the European Commission and based on the dossier submitted by the applicant, which must contain data on the composition and nutritional, toxicological and allergenic properties of the novel food, as well as information on the manufacturing processes and intended use (Dall'Asta 2022; Ververis et al. 2020). All novel food applications received by EFSA are publicly accessible via the EFSA Register of Questions (ROQ) database (<http://registerofquestions.efsa.europa.eu/roqFrontend/login?>), while all published technical reports on the risk assessment of these products are published in the EFSA Journal. In this procedure, the Member States are only informed, and the evaluation and authorization are the responsibility of the Commission and EFSA (<https://www.efsa.europa.eu/en/efsajournal/pub/6555>; <https://www.efsa.europa.eu/en/supporting/pub/en-6488>). The evaluation also includes consideration of possible effects on vulnerable groups, and the Commission has the power to introduce post-market monitoring requirements to monitor the use of the

authorized Novel Food to ensure that the use is within safe limits as established by the Authority's risk assessment.

While there are standardized and well-defined methods for the assessment of nutritional, microbiological and toxicological risks, the assessment of allergic risks of a new protein source is less straightforward. Food allergens are mainly proteins that may pose a risk due to de novo sensitization or cross-reactivity (Table 1) (Valenta et al. 2015). The effective detection of food allergens is complicated by the effects of different treatments and food matrices on allergen traces and by interference with specific markers in food. Therefore, the assessment of allergenic potential is a major bottleneck and one of the biggest limitations in the risk assessment of many novel food candidates (Dall'Asta 2022). As there is no recognized specific trait that can predict food allergy, all guidelines recommend a weight of evidence (WOE) approach based on various tests of a protein's allergenic potential (Verhoeckx et al. 2016). The current risk assessment of allergenicity is based on the characterization of the protein component of the food based on biochemical and immunological tests such as ELISA, protein/peptide microarray, immunofluorescence, radioimmunoassay, Western blotting, and immunohistochemistry (Bianco et al. 2022) (Figure 2).

Advances in the field of immunology and new sequencing techniques, as well as a deeper knowledge of allergens, including their structures, now make it possible to perform homology searches, i.e., the comparison of a protein of

interest with known allergens to identify similarities and prevent possible cross-reactivity. *In silico* searches for amino acid sequence homologies and/or structural similarities with known allergens are becoming an interesting alternative for the discovery of food allergens in novel foods. Search engines such as the local alignment algorithm FASTA (Pearson and Lipman 1988) or the Basic Local Alignment Search Algorithm (BLAST) (Altschul et al. 1990) can be used, with the standard threshold of 35% identity over at least 80 amino acids set by the FAO/WHO Scientific Advisory Panel in 2001 (Kedar et al. 2024) to query the databases for allergenic proteins, such as the Structural Database of Allergenic Proteins (SDAP) (<https://fermi.utmb.edu>), the allergen database of the World Health Organization and International Union of Immunological Societies (WHO/IUIS) (www.allergen.org) and Allergome (<http://www.allergome.org>), AllergenOnline (<http://www.allergenonline.org>), ALLFam (<http://www.meduniwien.ac.at/allfam/>), and the COMPARE database (<http://comparedatabase.org/>). In addition to crystallographic and NMR-based approaches, Liquid Chromatography-Mass Spectrometry (LC-MS) is also relevant for the quantification of allergens in food, as it provides key information for allergen labeling and verification of the effectiveness of safety management and is therefore regarded by food companies as the gold standard for the multiple detection of known allergens in complex matrices (Cunsolo et al. 2014). In recent years, nucleic acid-based methods, such as real-time PCR, microarrays and DNA biosensors, have also been developed, which offer high molecular specificity but are associated with complex sample preparation and can yield false positive results (Shin et al. 2022).

4. Conclusions

The introduction of new foods, as well as new technologies or new materials, undoubtedly requires society and its leaders to establish an ad-hoc regulatory framework that governs safe production processes, minimizing potential unknown problems for human health and the environment. This aspect is defined by scientists as “regulating the unknown” (Finck 2018), and requires policymakers to balance regulatory approaches between protection and innovation, between promoting research and benefiting society, and between social acceptance and government interference. Depending on the culture and legal system, the balance may shift and one factor may be favored over others. Regulation usually involves testing and a scientific evaluation of potential negative effects on health and the environment (Vapnek, Purnhagen, and Hillel 2021). Throughout history, many new foods, ingredients or methods of food production have come to Europe. Some foods may arouse initial aversion if they come from sources that are alien to Europeans, such as insects or algae, or are produced using radically new technologies, such as cultured meat. However, it is foreseeable that as more information becomes available, trust and openness will grow until use is normalized. Rigorous assessment of the safety of novel foods and the procedures required for authorization and market access can make an important contribution (Jaeger et al. 2022; Trajkovska Petkoska et al. 2021). To this end, it

is worth investing in food traceability technologies, and in effective communication on the safety and clarity of information provided to consumers, are worthwhile, so that novel foods can be integrated into the diet and add value to a new food culture (Hadi and Brightwell 2021).

Author contributions

Miazzi Monica Marilena: conceptualization, writing-original draft and writing-review and editing; Dellino Maria: conceptualization, visualization, writing-review and editing; Fanelli Valentina: visualization, editing; Mascio Isabella: visualization, editing; Nigro Domenica: visualization, editing; De Giovanni Claudio: writing-review and editing; Montemurro Cinzia: conceptualization, funding acquisition; All authors have read and agreed to the published version of the manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This study was supported by the Project funded under the National Recovery and Resilience Plan (PNRRP), Mission 4 Component 2 Investment 1.3 - Call for tender No. 341 of 15 March 2022 of Italian Ministry of University and Research funded by the European Union - NextGenerationEU; Award Number: Project code PE000000003, Concession Decree No. 1550 of 11 October 2022 adopted by the Italian Ministry of University and Research, CUP D93C22000890001, Project title “ON Foods - Research and innovation network on food and nutrition Sustainability, Safety and Security - Working ON Foods”.

References

- Adl, S. M., D. Bass, C. E. Lane, J. Lukeš, C. L. Schoch, A. Smirnov, S. Agatha, C. Berney, M. W. Brown, F. Burki, et al. 2019. Revisions to the classification, nomenclature, and diversity of Eukaryotes. *The Journal of Eukaryotic Microbiology* 66 (1):4–119. doi:10.1111/jeu.12691.
- Aguilera-Morales, M., M. Casas-Valdez, S. Carrillo-Domínguez, B. González-Acosta, and F. Pérez-Gil. 2005. Chemical composition and microbiological assays of marine algae *Enteromorpha* spp. as a potential food source. *Journal of Food Composition and Analysis* 18 (1):79–88. doi:10.1016/j.jfca.2003.12.012.
- Aidoo, O. F., J. Osei-Owusu, K. Asante, A. K. Dofuor, B. O. Boateng, S. K. Debrah, K. D. Ninsin, S. A. Siddiqui, and S. Y. Chia. 2023. Insects as food and medicine: A sustainable solution for global health and environmental challenges. *Frontiers in Nutrition* 10:1113219. doi:10.3389/fnut.2023.1113219.
- Alexander, P., C. Brown, A. Arneth, C. Dias, J. Finnigan, D. Moran, and M. D. Rounsevell. 2017. Could consumption of insects, cultured meat or imitation meat reduce global agricultural land use? *Global Food Security* 15:22–32. doi:10.1016/j.gfs.2017.04.001.
- Allai, F. M., K. Gul, Z. A. A. Azad, I. Zahoor, S. Nazir, and A. Manzoor. 2023. Safety aspects of nanomaterials in natural foods. In *Plant-based bioactive compounds and food ingredients*, 319–38. New York: Apple Academic Press. doi:10.1201/9781003372226.
- Altschul, S. F., W. Gish, W. Miller, E. W. Myers, and D. J. Lipman. 1990. Basic local alignment search tool. *Journal of Molecular Biology* 215 (3):403–10. doi:10.1016/S0022-2836(05)80360-2.
- Banach, J. L., E. F. Hoek-Van Den Hil, and H. J. Van Der Fels-Klerx. 2020. Food safety hazards in the European seaweed chain. *Comprehensive Reviews in Food Science and Food Safety* 19 (2):332–64. doi:10.1111/1541-4337.12523.

- Barbosa, M., G. Lopes, P. Valentão, F. Ferreres, A. Gil-Izquierdo, M. Pereira, and P. B. Andrade. 2018. Edible seaweeds' phlorotannins in allergy: A natural multi-target approach. *Food Chemistry* 265:233–41. doi:10.1016/j.foodchem.2011.12.032.
- Barennes, H., M. Phimmasane, and C. Rajaonarivo. 2015. Insect consumption to address undernutrition, a national survey on the prevalence of insect consumption among adults and vendors in Laos. *PLoS One* 10 (8):e0136458. doi:10.1371/journal.pone.0136458.
- Belluco, S., C. Losasso, M. Maggioletti, C. C. Alonzi, M. G. Paoletti, and A. Ricci. 2013. Edible insects in a food safety and nutritional perspective: A critical review. *Comprehensive Reviews in Food Science and Food Safety* 12 (3):296–313. doi:10.1111/1541-4337.12014.
- Benard, C., A. Cultrone, C. Michel, C. Rosales, J.-P. Segain, M. Lahaye, J.-P. Galmiche, C. Cherbut, and H. M. Blotière. 2010. Degraded Carrageenan causing colitis in rats induces TNF secretion and ICAM-1 upregulation in monocytes through NF- κ B activation. *PLoS One* 5 (1):e8666. doi:10.1371/journal.pone.0008666.
- Bianco, M., G. Ventura, C. D. Calvano, I. Losito, and T. R. Cataldi. 2022. A new paradigm to search for allergenic proteins in novel foods by integrating proteomics analysis and in silico sequence homology prediction: Focus on spirulina and chlorella microalgae. *Talanta* 240:123188. doi:10.1016/j.talanta.2021.123188.
- Bisen, P. S., R. K. Baghel, B. S. Sanodiya, G. S. Thakur, and G. B. K. S. Prasad. 2010. *Lentinus edodes*: A macrofungus with pharmacological activities. *Current Medicinal Chemistry* 17 (22):2419–30. doi:10.2174/092986710791698495.
- Bonaccorsi, G., G. Garamella, G. Cavallo, and C. A. Lorini. 2020. Systematic review of risk assessment associated with jellyfish consumption as a potential novel food. *Foods (Basel, Switzerland)* 9 (7):935. doi:10.3390/foods9070935.
- Borthakur, A., S. Bhattacharyya, A. N. Anbazhagan, A. Kumar, P. K. Dudeja, and J. K. Tobacman. 2012. Prolongation of carrageenan-induced inflammation in human colonic epithelial cells by activation of an NF κ B-BCL10 loop. *Biochimica Et Biophysica Acta* 1822 (8):1300–7. doi:10.1016/j.bbadis.2012.05.001.
- Bose, U., J. A. Broadbent, A. Juhász, S. Karnaneedi, E. B. Johnston, S. Stockwell, K. Byrne, V. Limvipuvadh, S. Maurer-Stroh, A. L. Lopata, et al. 2021. Protein extraction protocols for optimal proteome measurement and arginine kinase quantitation from cricket *Acheta domesticus* for food safety assessment. *Food Chemistry* 348:129110. doi:10.1016/j.foodchem.2021.129110.
- Bull, C., D. Belobrajdic, S. Hamzelou, D. Jones, W. Leifert, R. Ponce-Reyes, N. S. Terefe, G. Williams, and M. Colgrave. 2022. How healthy are non-traditional dietary proteins? The effect of diverse protein foods on biomarkers of human health. *Foods (Basel, Switzerland)* 11 (4):528. doi:10.3390/foods11040528.
- Cadinu, L. A., P. Barra, F. Torre, F. Delogu, and F. A. Madau. 2020. Insect rearing: Potential, challenges, and circularity. *Sustainability* 12 (11):4567. doi:10.3390/su12114567.
- Cardwell, G., J. F. Bornman, A. P. James, and L. J. Black. 2018. A review of mushrooms as a potential source of dietary vitamin D. *Nutrients* 10 (10):1498. doi:10.3390/nu10101498.
- Chassaing, B., T. Van de Wiele, J. De Bodt, M. Marzorati, and A. T. Gewirtz. 2017. Dietary emulsifiers directly alter human microbiota composition and gene expression *ex vivo* potentiating intestinal inflammation. *Gut* 66 (8):1414–27. doi:10.1136/gutjnl-2016-313099.
- Cheung, P. C. 2010. The nutritional and health benefits of mushrooms. *Nutrition Bulletin* 35 (4):292–9. doi:10.1111/j.1467-3010.2010.01859.x.
- Choudhary, B., O. P. Chauhan, and A. Mishra. 2021. Edible seaweeds: A potential novel source of bioactive metabolites and nutraceuticals with human health benefits. *Frontiers in Marine Science* 8:740054. doi:10.3389/fmars.2021.740054.
- Clark, A. J., B. K. Soni, B. Sharkey, T. Acree, E. Lavin, H. M. Bailey, H. H. Stein, A. Han, M. Elie, and M. Nadal. 2022. Shiitake mycelium fermentation improves digestibility, nutritional value, flavor and functionality of plant proteins. *LWT* 156:113065. doi:10.1016/j.lwt.2021.113065.
- Crippa, M., E. Solazzo, D. Guizzardi, F. Monforti-Ferrario, F. N. Tubiello, and A. Leip. 2021. Food systems are responsible for a third of global anthropogenic GHG emissions. *Nature Food* 2 (3):198–209. doi:10.1038/s43016-021-00225-9.
- Cunsolo, V., V. Muccilli, R. Saletti, and S. Foti. 2014. Mass spectrometry in food proteomics: A tutorial. *Journal of Mass Spectrometry: JMS* 49 (9):768–84. doi:10.1002/jms.3374.
- Dall'Asta, C. 2022. Why 'new' foods are safe and how they can be assessed. In *Novel foods and edible insects in the European Union*, ed. L. Scaffardi and G. Formici. Cham: Springer. doi:10.1007/978-3-031-13494-4_5.
- De Araujo, R. and Peteiro, C. 2021. Algae as food and food supplements in Europe. Luxembourg: Publications Office of the European Union. doi:10.2760/049515.JRC125913.
- Diaz, C. J., K. J. Douglas, K. Kang, A. L. Kolarik, R. Malinowski, Y. Torres-Tijj, J. V. Molino, A. Badary, and S. P. Mayfield. 2023. Developing algae as a sustainable food source. *Frontiers in Nutrition* 9:1029841. doi:10.3389/fnut.2022.1029841.
- Dobermann, D., J. A. Swift, and L. M. Field. 2017. Opportunities and hurdles of edible insects for food and feed. *Nutrition Bulletin* 42 (4):293–308. doi:10.1111/nbu.12291.
- Duvnjak, D., M. Pantić, V. Pavlović, V. Nedović, S. Lević, D. Matijašević, A. Sknepnek, and M. Nikšić. 2016. Advances in batch culture fermented *Coriolus versicolor* medicinal mushroom for the production of antibacterial compounds. *Innovative Food Science & Emerging Technologies* 34:1–8. doi:10.1016/j.ifset.2015.12.028.
- FAO and WHO. 2023. Summary report of the Ad hoc Joint FAO/WHO Expert Consultation on Risk Assessment of Food Allergens—Part 4: Review and establish exemptions for the food allergens (<https://www.who.int/news-room/events/detail/2022/11/14/default-calendar/ad-ho-c-joint-fao-who-expert-consultation-on-risk-assessment-of-food-allergens-part-4-review-and-establish-exemption-for-the-food-allergens>).
- Finck, M. 2018. Blockchains: Regulating the unknown. *German Law Journal* 19 (4):665–92. doi:10.1017/S2071832200022847.
- Geethangili, M., and Y. M. Tzeng. 2011. Review of pharmacological effects of *Antrodia camphorata* and its bioactive compounds. Evidence-based complementary and alternative medicine. *Evidence-Based Complementary and Alternative Medicine: ECAM* 2011 (1):212641. doi:10.1093/ecam/nep108.
- Goikoetxea, M. J., M. Fernández-Benítez, and M. L. Sanz. 2009. Food allergy to Shiitake (*Lentinus edodes*) manifested as oesophageal symptoms in a patient with probable eosinophilic oesophagitis. *Allergologia Et Immunopathologia* 37 (6):333–4. doi:10.1016/j.aller.2009.05.002.
- Hadi, J., and G. Brightwell. 2021. Safety of alternative proteins: Technological, environmental and regulatory aspects of cultured meat, plant-based meat, insect protein and single-cell protein. *Foods (Basel, Switzerland)* 10 (6):1226. doi:10.3390/foods10061226.
- Hall H., Fitches E., Smith R., 2021. Insects as animal feed: novel ingredients for use in pet, aquaculture and livestock diets. CABI, Oxfordshire, UK (2021), 138 pages. *Animal Bioscience* 2022; 35(1): 153–154. doi:10.5713/ab.22.0001B
- Hawksworth, D. L., and R. Lücking. 2017. Fungal diversity revisited: 2.2 to 3.8 million species. *Microbiology Spectrum* 5 (4):10–1128. doi:10.1128/microbiolspec.funk-0052-2016.
- He, X., and H. M. Hwang. 2016. Nanotechnology in food science: Functionality, applicability, and safety assessment. *Journal of Food and Drug Analysis* 24 (4):671–81. doi:10.1016/j.jfda.2016.06.001.
- Healy, L. E., X. Zhu, M. Pojić, C. Sullivan, U. Tiwari, J. Curtin, and B. K. Tiwari. 2023. Biomolecules from macroalgae—nutritional profile and bioactives for novel food product development. *Biomolecules* 13 (2):386. doi:10.3390/biom13020386.
- Hobbs, C. 2000. Medicinal value of *Lentinus edodes* (Berk) Sing (*Agaricomycetidae*). A literature review. *International Journal of Medicinal Mushrooms* 2 (4):16. doi:10.1615/IntJMedMushr.v2.i4.90.
- Imathiu, S. 2020. Benefits and food safety concerns associated with consumption of edible insects. *NFS Journal* 18:1–11. doi:10.1016/j.nfs.2019.11.002.
- Jaeger, S. R., S. L. Chheang, C. M. Roigard, and A. V. Cardello. 2022. Individual differences in food neophobia and private body consciousness influence product-elicited emotional valence and arousal. *Food Quality and Preference* 99:104566. doi:10.1016/j.foodqual.2022.104566.
- Kalač, P. 2009. Chemical composition and nutritional value of European species of wild growing mushrooms: A review. *Food Chemistry* 113 (1):9–16. doi:10.1016/j.foodchem.2008.07.077.

- Kedar, O., A. Golberg, U. Obolski, and R. Confino-Cohen. 2024. Allergic to bureaucracy? Regulatory allergenicity assessments of novel food: Motivations, challenges, compromises, and possibilities. *Comprehensive Reviews in Food Science and Food Safety* 23 (2):e13300. doi:10.1111/1541-4337.13300.
- Lafarga, T. 2019. Effect of microalgal biomass incorporation into foods: Nutritional and sensorial attributes of the end products. *Algal Research* 41:101566. doi:10.1016/j.algal.2019.101566.
- Leni, G., T. Tedeschi, A. Faccini, F. Pratesi, C. Folli, I. Puxeddu, P. Migliorini, N. Gianotten, J. Jacobs, S. Depraetere, et al. 2020. Shotgun proteomics, in-silico evaluation and immunoblotting assays for allergenicity assessment of lesser mealworm, black soldier fly and their protein hydrolysates. *Scientific Reports* 10 (1):1228. doi:10.1038/s41598-020-57863-5.
- Leyland, B., S. Leu, and S. Boussiba. 2017. Are Thraustochytrids algae? *Fungal Biology* 121 (10):835–40. doi:10.1016/j.funbio.2017.07.006.
- López-Pedrouso, M., J. M. Lorenzo, J. D. D. Alché, R. Moreira, and D. Franco. 2023. Advanced proteomic and bioinformatic tools for predictive analysis of allergens in novel foods. *Biology* 12 (5):714. doi:10.3390/biology12050714.
- Ma, Z., M. Mondor, F. G. Valencia, and A. J. Hernández-Álvarez. 2023. Current state of insect proteins: Extraction technologies, bioactive peptides and allergenicity of edible insect proteins. *Food & Function* 14 (18):8129–56. doi:10.1039/D3FO02865H.
- Mancini, M. C., and F. Antonioli. 2020. To what extent are consumers' perception and acceptance of alternative meat production systems affected by information? The case of cultured meat. *Animals: An Open Access Journal from MDPI* 10 (4):656. doi:10.3390/ani10040656.
- Marga, F. S., B. P. Purcell, G. Forgacs, and A. Forgacs. 2017. Edible and animal-product-free microcarriers for engineered meat. U.S. Patent No. 9,752,122. Washington, DC: U.S. Patent and Trademark Office.
- Matos, J., C. Cardoso, N. M. Bandarra, and C. Afonso. 2017. Microalgae as healthy ingredients for functional food: A review. *Food & Function* 8 (8):2672–85. doi:10.1039/C7FO00409E.
- Mazac, R., N. Järviö, and H. L. Tuomisto. 2023. Environmental and nutritional life cycle assessment of novel foods in meals as transformative food for the future. *The Science of the Total Environment* 876:162796. doi:10.1016/j.scitotenv.2023.162796.
- Mazac, R., J. Meinilä, L. Korkalo, N. Järviö, M. Jalava, and H. L. Tuomisto. 2022. Incorporation of novel foods in European diets can reduce global warming potential, water use and land use by over 80. *Nature Food* 3 (4):286–93. doi:10.1038/s43016-022-00489-9.
- McNamara, E., and C. Bomkamp. 2022. Cultivated meat as a tool for fighting antimicrobial resistance. *Nature Food* 3 (10):791–4. doi:10.1038/s43016-022-00602-y.
- Melgar-Lalanne, G., A. J. Hernández-Álvarez, and A. Salinas-Castro. 2019. Edible insects processing: Traditional and innovative technologies. *Comprehensive Reviews in Food Science and Food Safety* 18 (4):1166–91. doi:10.1111/1541-4337.12463.
- Mokaya, H. O., R. M. Ndunda, T. M. Kegode, S. J. Koech, C. M. Tanga, S. Subramanian, and B. Ngoka. 2023. Silkworm pupae: Potential and less exploited alternative source of nutrients and natural antioxidants. *Journal of Insects as Food and Feed* 9 (4):491–501. doi:10.3920/JIFF2021.0134.
- Murefu, T. R., L. Macheke, R. Musundire, and F. A. Manditsera. 2019. Safety of wild harvested and reared edible insects: A review. *Food Control*. 101:209–24. doi:10.1016/j.foodcont.2019.03.003.
- Muszyńska, B., A. Grzywacz-Kisielewska, K. Kała, and J. Gdula-Argasińska. 2018. Anti-inflammatory properties of edible mushrooms: A review. *Food Chemistry* 243:373–81. doi:10.1016/j.foodchem.2017.09.149.
- Nawaz, M. A., R. Mesnage, A. M. Tsatsakis, K. S. Golokhvast, S. H. Yang, M. N. Antoniou, and G. Chung. 2019. Addressing concerns over the fate of DNA derived from genetically modified food in the human body: A review. *Food and Chemical Toxicology: An International Journal Published for the British Industrial Biological Research Association* 124:423–30. doi:10.1016/j.fct.2018.12.030.
- Niego, A. G., S. Rapior, N. Thongklang, O. Raspé, W. Jaidee, S. Lumyong, and K. D. Hyde. 2021. Macrofungi as a nutraceutical source: Promising bioactive compounds and market value. *Journal of Fungi (Basel, Switzerland)* 7 (5):397. doi:10.3390/jof7050397.
- Oibiokpa, F. I., H. O. Akanya, A. A. Jigam, A. N. Saidu, and E. C. Egwim. 2018. Protein quality of four indigenous edible insect species in Nigeria. *Food Science and Human Wellness* 7 (2):175–83. doi:10.1016/j.fshw.2018.05.003.
- Ong, K. J., J. Johnston, I. Datar, V. Sewalt, D. Holmes, and J. A. Shatkin. 2021. Food safety considerations and research priorities for the cultured meat and seafood industry. *Comprehensive Reviews in Food Science and Food Safety* 20 (6):5421–48. doi:10.1111/1541-4337.12853.
- Pali-Schöll, I., K. Verhoeckx, I. Mafra, S. L. Bavaro, E. C. Mills, and L. Monaci. 2019. Allergenic and novel food proteins: State of the art and challenges in the allergenicity assessment. *Trends in Food Science & Technology* 84:45–8. doi:10.1016/j.tifs.2018.03.007.
- Palmer, L. K., J. T. Marsh, M. Lu, R. E. Goodman, M. G. Zeece, and P. E. Johnson. 2020. Shellfish tropomyosin IgE cross-reactivity differs among edible insect species. *Molecular Nutrition & Food Research* 64 (8):e1900923. doi:10.1002/mnfr.201900923.
- Parodi, A., A. Leip, I. J. M. De Boer, P. M. Slegers, F. Ziegler, E. H. M. Temme, M. Herrero, H. Tuomisto, H. Valin, C. E. Van Middelaar, et al. 2018. The potential of future foods for sustainable and healthy diets. *Nature Sustainability* 1 (12):782–9. doi:10.1038/s41893-018-0189-7.
- Pearson, W. R., and D. J. Lipman. 1988. Improved tools for biological sequence comparison. *Proceedings of the National Academy of Sciences of the United States of America* 85 (8):2444–8. doi:10.1073/pnas.85.8.2444.
- Petrus, M., R. Culerrier, M. Campistron, A. Barre, and P. Rougé. 2010. First case report of anaphylaxis to spirulin: Identification of phycocyanin as responsible allergen. *Allergy Eur. J. Allergy Clin. Immunol* 65 (7):924–5. doi:10.1111/j.1398-9995.2009.02257.x.
- Polikovskiy, M., F. Fernand, M. Sack, W. Frey, G. Müller, and A. Golberg. 2019. In silico food allergenic risk evaluation of proteins extracted from macroalgae *Ulva* sp. with pulsed electric fields. *Food Chemistry* 276:735–44. doi:10.1016/j.foodchem.2018.09.134.
- Post, M. 2014. Cultured beef: Medical technology to produce food. *Journal of the Science of Food and Agriculture* 94 (6):1039–41. doi:10.1002/jsfa.6474.
- Pravettoni, V., L. Primavesi, and M. Piantanida. 2014. Shiitake mushroom (*Lentinus edodes*): A poorly known allergen in Western countries responsible for severe work-related asthma. *International Journal of Occupational Medicine and Environmental Health* 27 (5):871–4. doi:10.2478/s13382-014-0296-2.
- Precup, G., E. Ververis, D. Azzollini, F. Rivero-Pino, P. Zakidou, and A. Germini. 2022. The safety assessment of insects and products thereof as novel foods in the European Union. *Novel Foods and Edible Insects in the European Union*, 123. Switzerland AG: Springer Nature. doi:10.1007/978-3-031-13494-4_7.
- Quintieri, L., C. Nitride, E. De Angelis, A. Lamonaca, R. Pilolli, F. Russo, and L. Monaci. 2023. Alternative protein sources and novel foods: Benefits, food applications and safety issues. *Nutrients* 15 (6):1509. doi:10.3390/nu15061509.
- Regulation (EU). 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods, amending Regulation (EU) No 1169/2011 of the European Parliament and of the Council and repealing Regulation (EC) No 258/97 of the European Parliament and of the Council and Commission Regulation (EC) No 1852/2001. <https://eur-lex.europa.eu/eli/reg/2015/2283/oj>
- Ribeiro, J. C., L. M. Cunha, B. Sousa-Pinto, and J. Fonseca. 2018. Allergic risks of consuming edible insects: A systematic review. *Molecular Nutrition & Food Research* 62 (1):1700030. doi:10.1002/mnfr.201700030.
- Ribeiro, J. C., B. Sousa-Pinto, J. Fonseca, S. C. Fonseca, and L. M. Cunha. 2021. Edible insects and food safety: Allergy. *Journal of Insects as Food and Feed* 7 (5):833–47. doi:10.3920/JIFF2020.0065.
- Routray, I., A. Mahmood, N. E. Ngwa, M. Tasleem, K. Sahin, O. Kucuk, and S. Ali. 2016. Cell line cross-contamination and accidental co-culture. *Journal of Stem Cell Research & Therapeutics* 1 (5):00031. doi:10.15406/jsrt.2016.01.00031.
- Ruggeri, M., F. D'Ascenzo, S. A. Prencipe, and G. Vinci. 2023. Edible insects as a novel food choice. European challenges. In *Tokyo summit 7-Tokyo 7th international innovative studies & contemporary scientific research congress proceedings book*, 28–36. ed. I. Pavlovic, M. Lopuzanska-Dawid

- Rzymiski, P., P. Niedzielski, N. Kaczmarek, T. Jurczak, and P. Klimaszuk. 2015. The multidisciplinary approach to safety and toxicity assessment of microalgae-based food supplements following clinical cases of poisoning. *Harmful Algae* 46:34–42. doi:10.1016/j.hal.2015.05.003.
- Saied, A. A., D. Chandran, H. Chopra, A. Dey, T. B. Emran, and K. Dhama. 2023. Cultivated meat could aid in reducing global antimicrobial resistance burden - Producing meat without antibiotics as a safer food system for the future. *International Journal of Surgery (London, England)* 109 (2):189–90. doi:10.1097/JIS9.000000000000199.
- Sans, P., and P. Combris. 2015. World meat consumption patterns: An overview of the last fifty years (1961–2011). *Meat Science* 109:106–11. doi:10.1016/j.meatsci.2015.05.012.
- Schlüter, O., B. Rumpold, T. Holzhauser, A. Roth, R. F. Vogel, W. Quasigroch, S. Vogel, V. Heinz, H. Jäger, N. Bandick, et al. 2017. Safety aspects of the production of foods and food ingredients from insects. *Molecular Nutrition & Food Research* 61 (6):1600520. doi:10.1002/mnfr.201600520.
- Shin, J. H., Y. V. M. Reddy, T. J. Park, and J. P. Park. 2022. Recent advances in analytical strategies and microsystems for food allergen detection. *Food Chemistry* 371:131120. doi:10.1016/j.foodchem.2021.131120.
- Singh, A., S. Garg, and A. K. Upadhyay. 2023. Identification and analysis of allergens in edible mushroom (*Agaricus bisporus*). *Materials Today: Proceedings* 106:36–40. doi:10.1016/j.matpr.2023.03.639.
- Stephens, N., L. Di Silvio, I. Dunsford, M. Ellis, A. Glencross, and A. Sexton. 2018. Bringing cultured meat to market: Technical, socio-political, and regulatory challenges in cellular agriculture. *Trends in Food Science & Technology* 78:155–66. doi:10.1016/j.tifs.2018.04.010.
- Tamang, J. P., K. Watanabe, and W. H. Holzapfel. 2016. Review: Diversity of microorganisms in global fermented foods and beverages. *Frontiers in Microbiology* 7:377. doi:10.3389/fmicb.2016.00377.
- Taylor, G., and N. Wang. 2018. Entomophagy and allergies: A study of the prevalence of entomophagy and related allergies in a population living in North-Eastern Thailand. *Bioscience Horizons: The International Journal of Student Research* 11: Hzy003. doi:10.1093/biohorizons/hzy003.
- The European Commission. Blue bioeconomy -Towards a strong and sustainable EU algae sector. Communication 2022. Accessed February 7, 2022. https://oceans-and-fisheries.ec.europa.eu/news/towards-strong-and-sustainable-eu-algae-sector-conclusions-public-consultation-2021-02-11_en.
- Trajkovska Petkoska, A., Daniloski, D. Kumar, N. Pratibha, and Broach, A. T. 2021. Biobased materials as a sustainable potential for edible packaging. In *Sustainable packaging. Environmental footprints and eco-design of products and processes*, ed. S. S. Muthu. Springer, Singapore. doi:10.1007/978-981-16-4609-6_5.
- Treich, N. 2021. Cultured meat: Promises and challenges. *Environmental & Resource Economics* 79 (1):33–61. doi:10.1007/s10640-021-00551-3.
- Truzzi, E., D. Bertelli, A. R. Bilia, G. Vanti, E. Maretta, and E. Leo. 2023. Combination of nanodelivery systems and constituents derived from novel foods: A comprehensive review. *Pharmaceutics* 15 (11):2614. doi:10.3390/pharmaceutics15112614.
- Turck, D., T. Bohn, J. Castenmiller, S. De Henauw, K. I. Hirsch-Ernst, and H. K. Knutsen, EFSA Panel on Nutrition, Novel Foods and Food Allergens. 2023. 2022. Scientific opinion on the safety of freeze-dried mycelia of *Antrodia*. *EFSA Journal* doi:10.2903/j.efsa.2023.8334.
- Tzachor, A., C. E. Richards, and L. Holt. 2021. Future foods for risk-resilient diets. *Nature Food* 2 (5):326–9. doi:10.1038/s43016-021-00269-x.
- UN. 2019. https://population.un.org/wpp/publications/files/wpp2019_highlights.pdf
- Valenta, R., H. Hochwallner, B. Linhart, and S. Pahr. 2015. Food allergies: The basics. *Gastroenterology* 148 (6):1120–31.e4. e4. doi:10.1053/j.gastro.2015.02.006.
- van Dijk, M., T. Morley, M. L. Rau, and Y. Saghai. 2021. A meta-analysis of projected global food demand and population at risk of hunger for the period 2010–2050. *Nature Food* 2 (7):494–501. doi:10.1038/s43016-021-00322-9.
- Vapnek, J., K. Purnhagen, and B. Hillel. 2021. Regulatory and legislative framework for novel foods. *Food formulation: Novel ingredients and processing techniques*, 285–308. Hoboken, New Jersey, US: John Wiley & Sons, Ltd. doi:10.1002/9781119614760.ch14.
- Varunjikar, M. S., I. Belghit, J. Gjerde, M. Palmblad, E. Oveland, and J. D. Rasinger. 2022. Shotgun proteomics approaches for authentication, biological analyses, and allergen detection in feed and food-grade insect species. *Food Control*. 137:108888. doi:10.1016/j.foodcont.2022.108888.
- Verhoeckx, K., H. Broekman, A. Knulst, and G. Houben. 2016. Allergenicity assessment strategy for novel food proteins and protein sources. *Regulatory Toxicology and Pharmacology: RTP* 79:118–24. doi:10.1016/j.yrtph.2016.03.016.
- Ververis, E., R. Ackerl, D. Azzollini, P. A. Colombo, A. De Sesmaisons, C. Dumas, A. Fernandez-Dumont, L. Ferreira da Costa, A. Germini, T. Goumperis, et al. 2020. Novel foods in the European Union: Scientific requirements and challenges of the risk assessment process by the European Food Safety Authority. *Food Research International (Ottawa, Ont.)* 137:109515. doi:10.1016/j.foodres.2020.109515.
- Wang, Y., S. Chen, Z. Yan, and M. Pei. 2019. A prospect of cell immortalization combined with matrix microenvironmental optimization strategy for tissue engineering and regeneration. *Cell & Bioscience* 9 (1):7. doi:10.1186/s13578-018-0264-9.
- Wasser, S. P. 2011. Current findings, future trends, and unsolved problems in studies of medicinal mushrooms. *Applied Microbiology and Biotechnology* 89 (5):1323–32. doi:10.1007/s00253-010-3067-4.
- Wells, M. L., P. Potin, J. S. Craigie, J. A. Raven, S. S. Merchant, K. E. Helliwell, A. G. Smith, M. E. Camire, and S. H. Brawley. 2017. Algae as nutritional and functional food sources: Revisiting our understanding. *Journal of Applied Phycology* 29 (2):949–82. doi:10.1007/s10811-016-0974-5.
- Warner, R. D. 2019. Analysis of the process and drivers for cellular meat production. *Animal: An International Journal of Animal Bioscience* 13 (12):3041–58. doi:10.1017/S1751731119001897.
- Yoshioka, Y., E. Kuroda, T. Hirai, Y. Tsutsumi, and K. J. Ishii. 2017. Allergic responses induced by the immunomodulatory effects of nanomaterials upon skin exposure. *Frontiers in Immunology* 8:169. doi:10.3389/fimmu.2017.00169.
- Zhang, L., Y. Hu, I. H. Badar, X. Xia, B. Kong, and Q. Chen. 2021. Prospects of artificial meat: Opportunities and challenges around consumer acceptance. *Trends in Food Science & Technology* 116:434–44. doi:10.1016/j.tifs.2021.07.010.