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# Cell-based Meat: An Emerging Paradigm in Fish Meat Production

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## Abstract

Cell-based fish meat production, an innovative technology in its early stages in India, promises to address the fish demands of the future. This method, unlike traditional fisheries, cultivates meat directly from cells. The process begins with harvesting progenitor cells from the target fish, then differentiating and proliferating to the required numbers (either with or without scaffolds), and finally, compacting them into meat. This technique has the potential to create meat of all types of fishes, including threatened, endangered and non-native species. However, before cell-based meat can be commercially viable in India, it faces challenges such as production costs, consumer preferences for meat quality, and the establishment of national food safety standards, particularly as the market readies for both imported and domestically produced lab-grown fish products.

**Keywords:** cellular agriculture, cultivated fish meat, *in vitro* meat, cell-based meat, food safety

## Introduction

The meat of aquatic animals, including finfish and shellfish, is nutrient rich and its consumption has been associated with several health benefits. Aquatic animals contribute to 17% of the total animal protein requirements of the human population. The demand for aquatic animal meat has been steadily increasing as evidenced by the increase in the *per capita* fish consumption from 9.9 kg in 1960s to 20.2 kg in 2022 and is expected to reach 21.4 kg by 2030 (FAO, 2022). The *per capita* fish consumption is expected to increase due to health-conscious dietary trends, urbanization, rising incomes and improved post-harvest practices (FAO, 2022).

The global aquatic animal production in 2020 was 178 million tonnes, contributed through capture fisheries (90.3 million tonnes) and aquaculture (87.5 million tonnes). Aquaculture has revolutionized fish meat production over the last few decades and is expected to reach a production of 100 million tonnes by 2027 and 106 million tonnes by 2030 (FAO, 2022). However, aquatic animal production, through capture fisheries is being affected by climate change, sustainability issues related to overfishing etc., while aquaculture is being affected by aquatic animal diseases, and food safety issues.

Cellular agriculture is beckoning the next revolution in aquatic animal meat production (Nyika et al., 2021; Soice & Johnston, 2021a). Cellular agriculture as the name implies, is the farming of cells. It operates at the cellular level as opposed to regular farming which operates at the animal / organism level. In this process, meat is grown from animal stem cells and is classified under the tissue engineering based cellular agriculture (Post, 2012, 2014; Datar et al., 2016; Post et al., 2020). Typically, the process involves growing animal cells in the laboratory to a desired cell number, followed by cell harvesting and compacting the cells as animal meat (Chriki & Hocquette, 2020; Reiss et al., 2021; Soice& Johnston, 2021b). The meat thus produced is known by different names such as cell-based meat, lab grown meat, cultivated meat, cultured meat, artificial meat, synthetic meat, clean meat, victimless meat, slaughter-free meat, cell cultured meat, test tube meat, *in vitro* meat, etc. FAO and WHO prefer the usage of cell-based meat (FAO & WHO, 2023)

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while the terms, cultured meat and cultivated meat are also frequently used (Bomkamp et al., 2022; Cai et al., 2024; Martins et al., 2024).

Meat produced *in vitro* through cellular agriculture potentially addresses ethical, environmental, and public health issues associated with conventional meat production (Bryant 2020; Treich, 2021). Growing demand for fish and shellfish has been met from the wild caught fishes and one third of fish stocks are over exploited in the last five decades. The latest technological advancements in *in vitro* meat production and large investments made in cellular agriculture by the global giants in food industry have the potential to reduce exploitation of farmed animal populations and their heavy carbon and other related pollution footprints and also play a role in preserving threatened wild species.

The world's first *in vitro* burger made from 20,000 lab-gown muscle fibers was reported in 2013 by Netherland's Mosa Meat (Post, 2014) and heralded a new dimension to the food sector. Worldwide, the investments in cell-based meat have risen from USD 250,000 in 2015 to USD 800 million in 2022. Research on cell-based meat has focussed on preparing different meat products such as beef, pork, chicken, foie gras, fish and shellfish products. Over the last decade several startups and companies across the world have focussed on cell-based meats (Cameron & O'Neill, 2019; Post et al., 2020; Rubio et al., 2020). The list, though not complete, includes companies from Netherlands (Mosa Meat, Meatable), United States of America (Eat Just, UPSIDE Foods, Memphis Meats, Mission Barns, Wild Type), United Kingdom (Cellular Agriculture Ltd., Multus Media, Biomimetic Solutions, Higher Steaks, Cellula Revolution), Israel (Believer Meats, Future Meat Technologies, Aleph Farms), Canada (Appleton Meats), Japan (Integriculture), Korea (Seawith) and Singapore (Shiok Meats). The companies producing cell-basedfish and shellfish meat include BlueNalu from USA (bluefin tuna), Finless Foods from USA (tuna), Wild Type from USA (salmon) and Shiok foods from Singapore (crustaceans) etc. In India, CSIR-Centre for Cellular and Molecular Biology (CCMB) and the Humane Society International (HSI), India are partnering to develop cell-based meat and the product is expected to come out in 2025. ICAR-Central Marine Fisheries Research Institute (CMFRI) is collaborating with Neat Meatt Biotech for developing lab-grown fish meat. ICAR-Central Institute of Fisheries Education (CIFE) has taken an initiative to employ cellular aquaculture to develop cultivated seafood. Clear Meat, a cell-based meat startup in India is working on chicken cells to produce chicken products such as EcoMeat® keema and EcoMeat® Steak.Globally, the market for cell-based meat is predicted to reach USD 2.1 billion in 2033 and would further increase to USD 13.7 billion by 2043 (https://www.idtechex.com/en/research-report/cultured-meat-2023-2043/913).

## Characteristics of cell-based meat:

- Cell-based meat is identical to the muscle cells that are present in conventional meat.
- Taste and texture of cell-based meat is akin to conventional meat.
- The taste and texture of cell-based meat closely resemble that of conventional meat.
- Cell-based meat can be produced without the necessity of slaughtering or killing animals.
- Cell-based meat production is an eco-friendly process compared to conventional meat production in terms of greenhouse emissions, land use and water use.
- Cell-based meat can be obtained from any terrestrial or aquatic animal species including threatened / endangered species.
- Cell-based meat can be prepared throughout the year irrespective of season.
- Cell-based meat can be produced at any location on the earth.
- Cell-based meat is produced under clean and hygienic laboratory facilities
- Cell-based meat is free from antibiotic residues and other contaminants associated with farmed terrestrial or aquatic species.
- Cell-based meat does not carry zoonotic bacteria or viruses.
- Regulatory approvals for cell-based meat are being initiated worldwide.

## The process of producing cell-based meat:

Fish meat comprises of myomeres (muscle tissue units) and myosepta (connective tissue sheaths). In order to achieve a product with nutritional and organoleptic characteristics similar to conventional meat, cell-based meat process should aim to recreate a tissue comprising primarily of muscle fibres (~90%) and small amounts of (~10%) fat and connective tissue (Listrat et al., 2016).

### Fin-fish Cell Lines:

The piscine cell lines are frequently employed for isolation of pathogenic viruses, toxicological examination of water and production of vaccines for protection of farmed aquatic animals (Lakra et al., 2011). The development of fish cell lines from commercially important fish has been continuing since the 1960s and presently 783 cell lines have been developed from various organs of different fish species (Swaminathan et al., 2021). The American Type Culture Collection (ATCC) and the European Collection of Authenticated Cell Cultures harbour 14 and 25 fish cell lines, respectively. In India, the National Repository of Fish Cell Lines (NRFC) maintains 50 cell lines of fish origin that are available for researchers for research and development purposes. However, non-deposition of all the developed fish cell lines in global or regional repositories is a major concern that hinders the dissemination of piscine cell lines for research purposes.

### Crustacean Cell Culture:

The research into developing cell lines from crustacean tissues is still in its early stages of emergence. Primary cell cultures have been developed from hepatopancreas, ovary, nerve, lymphoid and haematopoietic tissues of crustacean species (Sivakumar et al., 2019). However, improvements are needed in standardizing the methodologies for the isolation and maintenance crustacean cells; since, short-term cell cultures (obtained from repeated primary cell cultures) are suitable only for bench-scale research and not sufficient for cell-based meat applications. Research on long-term cell cultures is needed to meet the long-term goals of mass production and commercialization, due to the lack of established crustacean cell lines (Rinkevich, 2005). Therefore, concerted effort is required to derive and characterize crustacean cells for use in cell-based shrimp meat production.

### Basic Methodology for cell-based meat production:

Over 150 companies, investing nearly USD 2.6 billion, are striving to create a new standard for commercially manufacturing cell-based meat products. Cell-based meat production counts on advanced technological developments of cell lines, media formulation, and bioreactor design. A cell-based seafood production system involves (1) a suitable cell type; (2) media which provides essential nutrients for growth of cells; (3) a bioreactor for providing the suitable environment to produce the target cells at a large quantity; and (4) a 3D edible tissue scaffold to provide structure for cell-based seafood meat (Fig. 1).

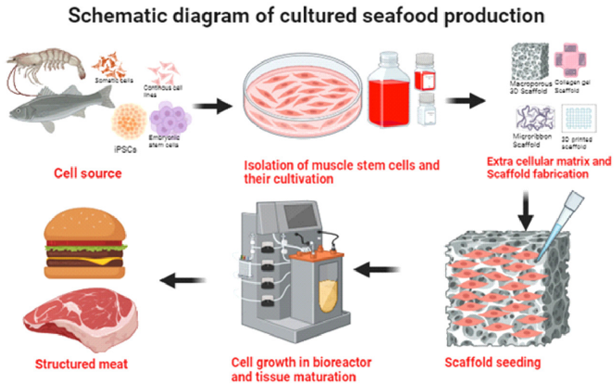


Fig. 1. Common steps involved in Cell-based seafood production (Created in Biorender.com)

The cell-based meat production process mimics the process of *in vivo* cell division and proliferation of skeletal muscle tissue (Bomkamp et al., 2022) and involves four major steps (Fig. 2). The first step is the isolation of stem cells from the animal whose meat is intended to be grown in the laboratory. The stems cells must be capable of differentiating into muscle cells, adipocytes and fibroblasts. The undifferentiated pluripotent stem cells are isolated either from the live animal through tissue biopsy or post-mortem, from the tissues of the slaughtered animal.

In the second step, the stem cells proliferation is carried out by immersing the stem cells in nutrient rich culture medium, where a single muscle cell can multiply to a trillion cells.

The third step is performed in a bioreactor for stem cell differentiation into muscle cells and proliferation of muscle cells. In some cases, scaffolds are used for cell attachment, nutrient diffusion to the cells and for the stimulation of extra-cellular matrix. The use of scaffolds helps the muscle cells to be arranged in a specific shape and texture, since the non-usage of scaffolds results in free floating muscle cells.

The fourth step is the product development. Muscle grown without any scaffold is useful for preparing unstructured meat products such as meat balls, meat nuggets meat burgers, etc., whereas muscle cells grown in the presence of scaffolds are useful for producing meat products with a specific shape and texture.

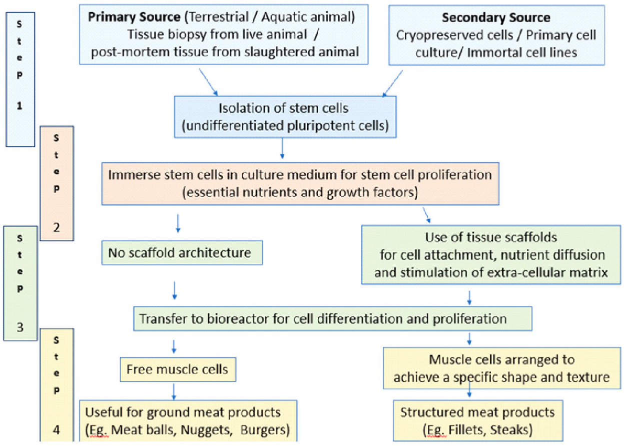


Fig. 2. Process flow of production of lab-grown meat

Two critical inputs for successful production of cell-based meat and that also have the potential to influence food safety are 'scaffolds' and 'foetal bovine serum'. In cell-based meat production, scaffolds are used not only to provide mechanical support but also to guide cell attachment and cell proliferation (Cai et al., 2020; Bomkamp et al., 2022; Lee et al., 2024). Scaffolds are either edible or non-edible type and both types stimulates the extra-cellular matrix composed of glycoproteins, collagen and enzymes. Non-edible scaffolds are removed at the end of the production process. However, edible scaffolds are retained in the cell-based meat. Scaffolds enable the production of textured thick meat by aiding oxygen and nutrient transport to the meat cells and helps in enhancing the textural qualities and appearance.The desirable properties of scaffolding materials are higher biocompatibility, degradability, cell adhesiveness, porosity and mechanical strength but lower immunogenicity. The biomaterials used for edible scaffolds are derived from plants (textured soy protein, wheat gluten, peanut protein, spinach leaves, celery, apple tissue, broccoli, floret, pectin), seaweeds (alginate), animals (collagen, gelatin, chitin, chitosan), fungi (mycelium), or synthetic materials (polyethylene glycol, polyglycolic acid, polystyrene, polyacrylamide). Technologies such as 3D bioprinting, electrospinning, extrusion, direct freezing, plant tissue decellularization, and cell sheet engineering are used for generating scaffolds (Mendes et al., 2017; Ben-Arye et al., 2020; Tanaka et al., 2022; Levi et al., 2022; Wang et al., 2023). Further research is needed for producing edible scaffolds that are sustainable, scalable and does not affect the meat taste.

Foetal Bovine Serum (FBS), as the name indicates, is obtained from the foetus of pregnant cows at the time of slaughter. FBS is a crucial ingredient of the media used for cell-based meat productions as it plays a key role in cell adhesion, cell proliferation and cell maintenance (Koblinski et al., 2005; Brunner et al., 2010). FBS is generally used at 10-20% level for cell proliferation and at 0.5 to 2% level for cell differentiation (Bhat et al., 2019; Kolkmann et al., 2020). The major components of FBS are serum proteins, transport proteins, enzymes, hormones, growth factors, cytokines, fatty acids, lipids, vitamins, minerals and inorganic compounds. The high cost, supply shortages, ethical concerns and food safety aspects related to FBS has propelled the research on FBS replacers (Piletz et al., 2018; Tancharoen et al., 2019). Researchers have tried several alternatives such as chick embryo extracts, bovine milk, colostrum, platelet lysates, pituitary extracts, bovine ocular fluids, plant proteins, fish serum, cocoon sericin, earthworm coelomic fluid, as FBS replacers for the growth of different cell types (Chelladurai et al., 2021). Substances that were used as FBS replacers for the growth of bovine, ovine, porcine and avian cells include transforming growth factor (TGF-β3), bovine serum albumin, insulin, transferrin, selenium, glucose, fructose, glycine, sericin, and polyvinyl chloride (Lee et al., 2022).

## Food Safety issues pertaining to the production of cell-based meat

Several food safety issues (Table 1) must be addressed during the different steps of the cell-based meat production (Ong et al., 2021; Stout et al., 2022; Naraoka et al., 2024) to ensure that the final product is safe for human consumption.

A comprehensive grasp of the cell-based meat production process is crucial for identifying potential food safety hazards and devising suitable control strategies. The principles of the existing HACCP based food safety system being practiced in the conventional meat processing may be applied to the cell-based meat production process.

## Commercial production of cell-based fish meat:

The world's first *in vitro* burger was revealed to the general public by Netherland's Mosa Meat in 2013 (Post, 2014). Later several startups have ventured into the field of cell-based beef (e.g. Aleph Farms, Meatable, Memphis meat, Mosa Meat), pork (e.g. High Steaks, New Age Meats), chicken (e.g. Cubiq Food, Eat Just, Super Meat), foie gras (e.g. Gourmey, Integriculture). The cell-based fish meat producers are listed in Table 2.

Table 1. Food safety concerns and action points for safe production of cell-based fish meat

| Production step | Food safety Concern | Action Points |
|---|---|---|
| Step 1: Isolation of stem cells | • Health status of the animal from which the cells are sourced.<br>• Enzymes/chemicals used for cell liberation, and cell preservation (cryoprotectants such as DMSO, sorbitol, inulin). | • Collection of cells from animals that are free from zoonotic diseases.<br>• Development of cell lines suitable for cell-based meat production. |
| Step 2: Stem cell proliferation | • Chemicals/nutrients used for cell proliferation (amino acids, vitamins, minerals, growth factors, antibiotics, etc. The media requirements are specific to the type of meat cells that are being grown).<br>• Foetal bovine serum (FBS) is an important component of the culture media but FBS might harbour microbial contaminants and endotoxins (Wessman & Levings, 1999). | • Various components of the culture media must be assessed from the food safety point of view.<br>• Development of alternatives to FBS or employing serum-free culture medium |
| Step 3: Cell differentiation in a bioreactor | • Use of growth factors such as TGF, FGF, IGF for cell differentiation, oxygen carriers such as haemoglobin, myoglobin, perflurochemicals. Use of enzymes/ chemicals (trypsin, EDTA) during cell harvesting.<br>• Nutrient rich culture media are vulnerable to contamination with bacteria (Mycoplasma).<br>• Scaffolds are moulds to which the cells get attached to achieve a certain shape. Different types of natural and synthetic materials are used for producing edible and non-edible scaffolds. | • The growth factors and other components of the culture media must be assessed for food safety.<br>• Develop standard operating procedures to avoid bacterial contamination during cell-based meat production.<br>• The edible scaffolds must not cause injury or allergy or any other harm to the consumers.<br>• Non-edible scaffolds must be biodegradable. |
| Step 4: Fish meat product development | • Muscle grown without any scaffold is useful for preparing unstructured meat products such as fish balls, fish nuggets, fish burgers, etc.<br>• Muscle cells grown in the presence of scaffolds are useful for producing meat products with a specific shape and texture.<br>• Unhygienic handling practices during cell harvesting results in bacterial contamination. | • Develop standard operating procedures to avoid bacterial contamination during cell-based meat product production. |

Table 2. Cell based fish meat producers

| Country | Startup / Company | Target Fish Species |
|---|---|---|
| USA | BlueNalu | Blue Fin Tuna |
| USA | Finless Foods | Tuna |
| USA | Wild Type | Salmon |
| Singapore | Shiok Foods | Crustaceans |

## Regulations for sale of cell-based meat:

The regulatory approvals for lab-grown meat have just begun (Stephens & Ellis, 2020; Ramesh & Mahajan, 2022). In 2020, Singapore was the first country that granted regulatory approval to cell-based meat product. Singapore Food Agency (SFA) has granted the approval for commercialization to Eat Just company for its lab-grown chicken product (GOOD Meat product). Following this, in 2022, the FDA gave pre-market approval to UPSIDE Foods for cell-based chicken meat products indicating that the product is safe to eat. In the United States, the pre-harvest processes regulated by the Food and Drug Administration (FDA) and the post-harvest processes are regulated by the United States Department of Agriculture (USDA). Further, UPSIDE Foods must receive approval from USDA before serving the cell-based meat products to the consumers. The gradual acceptance of cell-based meat by the food regulatory agencies worldwide is expected in the coming years. The Novel Foods Regulation (EU 2015/223) of the European Union ensures that new foods are safe for human consumption in Europe (Froggatt & Wellesley, 2019; Verzijden, 2019). In India, Food Safety Standards Authority of India (FSSAI) provides food safety guidance for all types of food including fish and fishery products (FSSAI, 2011, 2017) but as on date there is no specific standard for cell-based meat.

## Challenges:

- The cost of production of cell-based meat is high compared to the conventional meat and the foremost challenge is to offer cell-based meat at a reasonable price. The cost of the first *in vitro* burger grown from cow stem cells for three months, costed USD 330,000. Mosa Meat, Netherlands has presently brought down the cost to USD 30 per pound. Believer Meats, Israel expects to bring down the cost of a pound of lab-grown chicken meat to USD 7.70.
- Cell-based meat production requires educated man-power with specialized skills different from regular plant and animal food production systems.
- The cell-based meat needs to meet the consumer demands related to taste, texture, flavour and mouth feel that is natural to that of conventional meat.
- Developing disease free cell lines, safe culture media components, and low-cost bioreactor models are necessary for profitable and safe cell-based fish meat production.
- Develop standard operating procedures for cell-based fish meat production.
- Develop cell-based meat production of fish and shellfish species with high consumer demandincluding threatened, endangered and non-native species.
- Develop cell-based fish meat with pre-determined nutritional profile (e.g. rich in Omega-3 fatty acids, rich in antioxidants, low content of saturated fatty acids etc.)
- There is an urgent need to develop food safety standards for cell-based meat as it is expected that both imported and domestic lab-grown meat products would be ready for introduction into the markets globally in the near future.

The price of culture media is the single most important driver of the cost of cell-based meat as it accounts for 55-95% of the final cost (Garrison et al., 2022; Hubalek et al., 2022). Large volumes of media (~ 20000 L to generate 1000 kg of meat) are needed to produce the required number of meat cells (Specht, 2020; Chen et al., 2022). The cost of culture media is in turn influenced by FBS (for serum-based media) and TGF- β3 (for serum-free media). Continuous and dedicated research efforts are necessary to develop low-cost serum-free media for managing the production cost of cell-based meat. Focussed search is needed for identifying proteins from terrestrial plants, aquatic plants, insects and microorganisms for incorporation in cell culture media. Protein hydrolysates produced from fin-fish and crustacean processing waste are potential ingredients for use in cell culture media. Recycling of cell culture media or recovering unused components might be a zero-waste approach for cost cutting.

Consumer perception regarding cell-based meat is likely to be influenced by the information available (To et al., 2024) in print, electronic and social media. Hence, the public in general and meat consumers in particular have to be made aware of the production process, nutritional profile and food safety aspects of cell-based meat to ward of any misconceptions and apprehensions. A survey on the consumer perceptions in India indicated that 56.3% expressed very or extremely likely to try cell-based meat, whereas 32.9% expressed somewhat or moderately likely willingness to purchase cell-based meat (Bryant et al., 2019) indicating potential market for cell-based meat in India.

## Conclusion:

Cell-based fish meat products opens up new avenues that could positively influence the supply of fish meat regardless of geographic and seasonal constraints. This technology is capable of producing meat with customised nutrient profiles and from a wide variety of fishes. Reduced land use and thereby emissions is another major highlight of this new technology. Despite the emergence of several cell-based fish products globally, this innovative method of food production is still in its infancy in India. A dedicated research focus is essential to overcome challenges such as affordability, consumer acceptance and food safety to make cell-based fish meat a practical option for consumers. Developing cheaper alternatives for production of cell-based meat and addressing food safety issues will remain the critical issues that needs to be addressed immediately for successful commercialization of this technology.

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