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Cellular Fish Meat Production: Prospects and Challenges

NATIONAL ACADEMY OF AGRICULTURAL SCIENCES, NEW DELHI
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Preface

The world is seeking sustainable food alternatives to feed a projected 10 billion world population by 2050. Cellular fish meat production using muscle cell culture is a promising alternative to conventional meat and its importance has grown over the past decade. As the field is gaining prominence in India, attention of experts, high-level policymakers and regulatory agencies is highly required to foster the cultivated fish meat production sector. Recently, the Department of Biotechnology (DBT) has included smart proteins under BioE3 policy and has not only organised a series of webinars for popularising BioE3 policy, but also called for proposals for the establishment of bio-manufacturing hubs covering functional foods and smart proteins including cellular meat. In this backdrop, a brainstorming session titled 'Cellular Fish Meat Production: Prospects and Challenges' was convened by the National Academy of Agricultural Sciences (NAAS) on September 20, 2024 to explore the current knowledge related to cellular fish meat production, address the food safety considerations for cell-based food products and with an ultimate goal of developing policy recommendations to facilitate the commercial level cell-based fish meat production in India.

This Policy Paper is an outcome of the discussion during the brainstorming session. I am confident that the well-crafted recommendations in this Policy Paper will be embraced by all stakeholders and contribute to fully harnessing the potential for commercial cellular fish meat production in the country. On behalf of the Academy, I thank the Conveners (Dr. C.N. Ravishankar, Former Director, ICAR-Central Institute of Fisheries Education (CIFE), Mumbai and Dr. A. Gopalakrishnan, Former Director, ICAR-Central Marine Fisheries Research Institute (CMFRI), Kochi), Co-convener (Dr. Mukunda Goswami, Principal Scientist, ICAR-CIFE, Mumbai) and the participants including Dr. K.S. Sobhana (Principal Scientist and Head, CMFRI, Kochi) for their valuable inputs. Further, I place on record my appreciation and thanks to the Reviewers, Dr. W.S. Lakra and Dr. G. Jeyasekaran, and the Editors, Dr. V.K. Baranwal and Dr. R.K. Jain, for their sincere efforts in bringing out this document in the present form.

June 2025
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(Himanshu Pathak)
President, NAAS

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1. INTRODUCTION

About 89% of the total 157.4 million tonnes (Mt) of annual aquatic animal production is used for human consumption. This aligns with a global per capita fish consumption rate of 20.2 kg per year by approximately 7.8 billion people. It is estimated that by 2050, capture fisheries and aquaculture production are projected to reach 98.3 and 140 Mt, respectively (FAO, 2022). The future fish production is expected to rely mostly on aquaculture, which faces many key challenges for sustainable production. Hence, critical efforts will be required to provide larger volumes of feed to support aquaculture, to maintain quality of aquatic environments, to reduce pressure on wild aquatic organisms used for food and to provide quality aquatic foods to consumers (Aulakh *et al*., 2013; Ward and Signa, 2014; Abualtaher and Bar, 2020). These challenges led to exploring alternative environment friendly and sustainable sources of aquatic food through cell-based cultivation approaches (Goswami *et al*., 2022, 2024). Cellular meat also referred to as 'lab-grown meat/*in vitro* meat' has emerged as a promising supplement to conventional meat production, gaining significant importance over the past decade. Cellular fish meat has the potential to alleviate these fish sourcing challenges, with a focus on production efficiency, scalability, and controlled cultivation environments to address food security concerns. The cellular meat production process consists of four phases *i.e*., cell isolation and initial expansion, large scale expansion, tissue maturation and processing into a food product (Bomkamp *et al*., 2022). Advancing cellular fish meat production towards commercialisation requires robust academic research to overcome challenges and to drive innovation (Dolgin, 2019).

The importance of developing cellular meat has grown significantly in recent years leading to global interest and a doubling of investments in this sector over the past few years. This highlights the urgent need for further research and development in the emerging field of cellular meat production. Although a significant amount of basic research has been conducted in the recent past on cellular meat, most of it has focused on animals such as cattle, pig and chicken. Relatively less research has been carried out on fish despite it being an important source of animal protein and having cell physiology uniquely suited to *in vitro* cultivation. Cellular fish meat production presents a promising alternative for producing fish protein to meet the growing demand of the ever-increasing world population. This innovative biotechnological approach offers a sustainable, climate resilient and ethical solution, addressing the challenges associated with conventional fish farming (Goswami *et al*., 2024). However, the development and characterization of appropriate muscle cell lines from food fish species is crucial for advancing cellular fish meat production. In addition to the scope of providing alternative

source of protein to feed the burgeoning global population, cellular aquaculture offers enormous innovative opportunities. The recently launched BioE3 policy by the Govt. of India emphasizes the importance of sustainable and efficient utilisation of bioresources to facilitate innovation, scale-up and biomanufacturing of smart proteins (DBT, 2024).

Realising the importance of cellular fish meat, the National Academy of Agricultural Sciences (NAAS) organised a brainstorming session on 'Cellular Fish Meat Production: Prospects and Challenges'. This policy paper on cellular fish meat is the outcome of the deliberations in the brainstorming session and explores the need for cellular fish meat, identifies key challenges and provides strategic recommendations to promote its development and expansion in the country.

2. RELEVANCE OF CELLULAR FISH MEAT PRODUCTION

The global interest and importance of developing cellular meat has grown tremendously in recent years resulting in doubling of investments in this sector in the recent past. This surge highlights the increasing demand for research and development, particularly in the area of cellular fish meat production. To accelerate the path of cellular meat from innovation to market, robust academic research is indispensable. Although a significant amount of basic research has been conducted in the recent past on cellular meat, much of the focus has been on terrestrial animals, with relatively little attention given to fish which is an equally important source of quality animal protein. The cellular fish meat production offers a sustainable, climate resilient, ethical and biotechnological alternative to conventional fish farming and capture fisheries, addressing many of its inherent challenges. In addition to the scope of providing alternative source of protein to feed increasing world population, cellular fish meat holds immense potential for innovation, paving the way for novel applications and benefits in the food and biotechnology sectors.

3. PRESENT STATUS OF CELLULAR FISH MEAT PRODUCTION

The National Aeronautics and Space Administration (NASA), USA, supported the first research programme on *in vitro* edible muscle protein production from goldfish, in order to provide a sustainable and nutritious food source for space travellers during long-term manned space exploration missions (Benjaminson *et al*., 2002). However, a deeper understanding of muscle cell and tissue culture is essential to unlock the full potential of cellular fish meat production. To date, only a limited number of fish muscle cell lines have been successfully developed (Zhao *et al*., 2004; Zhao and Lu, 2006; Lai *et al*., 2008; Kumar *et al*., 2016). Notable exceptions include muscle cell lines developed from *Wallago attu* (Dubey *et al*., 2015) and olive flounder *Paralichthys olivaceus* (Peng *et al*., 2016) as well as myosatellite cells developed from the primary muscle tissue culture of common carp (Koumans *et al*., 1990) and rainbow trout (Powell *et al*., 1989) to delineate the controls on growth and differentiation of skeletal muscle. The prospects of cell-based fish meat rely on the development of appropriate

muscle cell lines, optimization of growth media, and scalable mass production of cells (Rubio *et al*., 2019). The interesting possibility of cultured meat was first demonstrated in 2013, when the world's first cell-cultured hamburger was produced at Maastricht University, in the Netherlands (Post *et al*., 2023). This breakthrough sparked global interest and cellular meat became an active area of research globally, driving advancements in the science of alternative proteins. In May 2023, 'Steakholder Foods', a start-up based in Israel, teamed up with a Singapore-based company, 'Umami Meats' and produced the 3D-printed cut of grouper fillet for the first time (https://edition.cnn.com/travel/article/steakholder-foods-3d-printed-cultivated-fish-fillet-spc-intl/index.html). The fillets were grown from cultivated grouper tissue in bioreactors in a lab using stem cells. These stem cells differentiated into muscle and fat cells ('bio-ink') and these were placed into cartridges in the 3D fish printer HD144 which built the fish meat in layers. The printing process allowed the steaks to be customizable by giving consumers the option of picking the fat composition of their cut and the 3D-printed fish had an exactly similar taste and flaky texture to real original grouper meat. It is expected that more endangered/wild caught species will be added to the process for large scale production in the coming years.

Development and characterization of fish muscle cell lines are critical for advancing cellular aquaculture. *In vitro* models, such as the immortalized mouse skeletal muscle myoblast cell line (C2C12), have been extremely useful for expanding knowledge about molecular mechanisms of muscle growth and differentiation in mammals (Yaffe and Saxel, 1977). However, similar studies in teleost fish remain in their infancy stage due to limited availability of equivalent permanent muscle cell lines. Though a few fish muscle cell lines have been developed so far, those have not been utilized for cellular fish meat production. The prospects of cell-based fish meat production rely on key factors such as the development of appropriate fish muscle cell lines, optimization of cell growth conditions, and the mass production of cells in bioreactors.

ICAR-Central Institute of Fisheries Education (CIFE), Mumbai has initiated research on cellular fish meat production through an international project entitled "*In-vitro* differentiation and characterization of fish muscle and optimization on plant-based scaffolding towards whole-cut seafood". This initiative undertaken in collaboration with Virginia Polytechnic Institute and State University (VT), USA, is funded by the Good Food Institute (GFI), USA. ICAR-CIFE, Mumbai is taking a lead in this endeavour and developed a continuous muscle cell line from rohu (*Labeo rohita*), one of the most important Indian Major Carps. The cell culture facility at ICAR-CIFE, Mumbai has been recognised as the National Smart Protein Innovation Hub on Cultivated Seafood by the GFI. Appropriate cell types have been characterised and cells have been optimised to grow on scaffolds for further development of cellular fish meat. Building on a robust background in marine fish cell lines research with 16 fully characterized immortal marine fish cell lines, the ICAR-Central Marine Fisheries Research Institute (CMFRI), Kochi has signed an MoU with Neat Meatt Biotech Pvt. Ltd., New Delhi to advance

cell-based seafood initiative. The collaboration focuses on scaling up bioreactor-based production and developing animal serum-free media formulations tailored to meet the nutritional requirements of immortal marine fish fibroblasts grown *in vitro.* Other ICAR fisheries institute like ICAR-Directorate of Coldwater Fisheries Research (DCFR), Bhimtal, has also initiated work on cellular fish meat.

Over the past two years, the Govt. of India has shown increasing interest in the country's potential to rise in the smart protein (globally referred to as alternative protein) sector. Recognized as one of the six priority areas in high-performance biomanufacturing, 'smart protein' has been identified as a key sector for advancing biotechnology excellence in India. In August 2023, the Department of Biotechnology, Government of India announced the formation of 'Sectoral Expert Committee on Biomanufacturing: Smart Proteins' to address technological and regulatory challenges faced by researchers and industry players actively involved in the smart protein sector. As the field of smart proteins gains momentum, this may be the ideal time to convene a focused gathering of scientists, high-level policymakers and regulatory experts, to facilitate in-depth policy deliberations on government investment in smart proteins and regulatory approval for novel foods, including cellular fish meat.

4. KEY CHALLENGES

The lack of appropriate well-characterised fish muscle cell lines, optimised serum-free and differentiation media, suitable scaffolds and other food grade reagents, along with suitably designed bioreactors for scaling up fish muscle cell cultures, are the major challenges in cellular aquaculture. Proper understanding of *in vitro* myogenesis in fish muscle culture is lacking which hinders the development of stable continuous muscle cell lines. The immortalization of fish muscle stem cell cultures remains a major challenge. Foetal Bovine Serum (FBS) is one of the most important factors which determines production cost as well as consumer safety and acceptance in cellular fish meat production. Presently, alternate growth supplements to FBS are still in the experimental stage and not yet commercially available. While fish muscle cell culture is presently feasible at the lab stage, scaling up production in bioreactors to meet industrial demand remains a major challenge. There is lack of appropriate bioreactor designs and innovations to support large-scale cultivation of fish muscle cells.

The Food Safety and Standards Authority of India (FSSAI) is yet to formulate specific standards and regulatory guidelines for smart protein products including cellular fish meat. As a result, these smart protein products are classified on the basis of ingredients used and technologies employed in the production process, aligning with existing regulations. The lack of clear guidelines poses a major challenge in preparing the necessary dossiers for regulatory approval of cellular fish meat for human consumption. Addressing these gaps is essential to facilitate commercialisation and regulatory acceptance of cellular fish meat products.

5. SAFETY ISSUES

As commercial cell-based food production continues to expand, addressing food safety concerns becomes an urgent priority, before these products reach the market. Recognizing this urgency, the Food and Agriculture Organization of the United Nations (FAO), in collaboration with the World Health Organization (WHO) has developed a comprehensive document to engage with member countries and relevant stakeholders (FAO & WHO, 2023). This initiative aims to proactively share current knowledge and identify concrete strategies to inform consumers and other stakeholders about the food safety considerations for cell-based food products. The alternative protein sector has witnessed significant progress following the expert consultation meeting organised by the FAO in Singapore in 2023. The Govt. of India has also started recognizing the country's potential to lead in the alternative protein sector (or 'smart protein' according to the government), particularly in fermentation-derived and cell-based food applications. Things have finally begun to gain momentum and multiple government-sponsored events with dedicated panel discussions on alternative proteins are happening every year such as World Food India and Global Bio-India. This growing focus signals a promising future for India in the smart protein sector.

While hazards have been identified in conventionally produced food, greater attention must be directed towards the specific materials, inputs, ingredients (including potential allergens), and equipment that are specific to cell-based food production, across all stages from cell selection, large scale biomass production to harvesting, processing and final product formulation. Any identified hazard at any stage must be thoroughly assessed with its potential consequences to human health clearly described. Generating and sharing comprehensive data on these hazards at the global level is essential to promote transparency and to build trust among stakeholders, enabling their positive engagement and support for the safe development of cell-based foods. Testing measures and methods for authenticating the purity of cell-based products intended for human consumption should be developed in laboratories. Detailed studies are needed to evaluate the presence of hazards in cell-based food products relative to other conventional food products. Proper labelling with detailed information is essential before these products are released for human consumption. Identification of causal chains of potential hazards at each stage of production and implementation of effective mitigation measures to control contamination are critical steps in ensuring safety and consumer trust in cell-based foods.

Effective food safety communication and building consumer trust are crucial for the successful adoption of novel foods. Addressing food safety questions transparently and providing reliable information can help to establish trust in the food safety regulatory system. International collaboration is essential, particularly for food safety authorities in low-and middle-income countries, enabling them to adopt evidence-based approaches and develop appropriate regulatory frameworks (FAO & WHO, 2023).

6. KEY RECOMMENDATIONS

- Prioritization of fish species for cellular fish meat development as well as promotion of research and development on cellular fish meat production in the country based on a thorough understanding of the cell-based meat development process.
- Establishment of dedicated facilities and the creation of a cohesive environment to support the development of cellular fish meat in the country through enhanced international collaborations.
- Generation of required data and preparation of a comprehensive dossier to secure regulatory approval for the safe consumption of cell-based fish meat.
- Formulating a robust regulatory framework to facilitate the approval of cellular fish meat for human consumption.
- Collecting insights and experiences from cell-based fish meat developers and producers, to update relevant food safety considerations, aiding competent authorities in conducting effective risk assessments and to refine regulatory compliance requirements to facilitate ease of business and support efficient scaling up of operations.
- Scaling up the cell-based fish meat production process through public-private partnership (PPP) mode to drive industrial expansion, accelerate market entry and promote the development of bio-foundries.
- Development of suitable alternatives and food grade reagents to replace FBS ensuring broader acceptability for cellular fish meat.

It is a fact that cellular fish meat production is still in its early stages of development. There is growing research interest in academic laboratories, and a growing corporate effort primarily driven by start-up companies worldwide, to address the increasing consumer demand for fish as food. At this stage, the efforts are focused on identifying suitable cell sources, optimizing media and developing scaffolding techniques. Over time, these efforts are expected to evolve towards scaling production to achieve meaningful impact. A visionary approach to cellular fish meat production offers the potential for safer and healthier alternatives for consumers, while enhancing environmental sustainability goals. For this emerging industry to realize its potential, government support for research and commercialization is crucial. Basic research is needed to better understand piscine and invertebrate cell types, differentiation processes, and metabolic requirements (Goswami *et al*., 2024). Public funding of research on cell-based fish meat can help reduce duplication of efforts, establish a strong foundation for commercial initiatives, and benefit the field. Creating awareness about the potential and challenges of cellular fish meat, while fostering a cohesive environment involving all stakeholders is the need of the hour.

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