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Technological Aspects of Bridging the Gap Between Cell-Based Food and Conventional Meat

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Abstract: Cell-based food, including cultured meat, introduces an innovative complement to our dietary options, introducing cellular agriculture and tissue engineering on the meat market together with traditional livestock farming. Originating from medical tissue cultivation techniques, this approach is now tailored for food production, prioritizing cost-effectiveness, palatability, and resource efficiency. As technology strives to efficiently upscale production, consumer acceptance stands as a key factor in adopting this new protein source. This review explores advances in cultivating muscle and fat tissues *in vitro*, emphasizing the importance of achieving muscle maturity, innovating scaffolds, and optimizing media composition to closely replicate the qualities of meat. It also addresses quality assessments of cultured meat based on its texture, nutritional content, and flavor. A concise examination of consumer perceptions reveals that acceptance is influenced by a blend of cultural, psychological, and social factors, balancing the positive potential outlook on cultured meat's benefits for society, the environment, and animal welfare against concerns about its unnaturalness, uncertainty, and safety. Demographic trends suggest higher acceptance among younger, well-educated and urban individuals, contrasting with reservations from those more familiar with the traditional meat sector. Addressing these varied viewpoints is essential for a better understanding of public acceptance if cultured meat is effectively introduced into our future food systems. As media interest in this alternative is still high, aligning technological developments with consumer expectations is crucial for the potential market introduction of cultured meat.

Key words: cell-based food, cultured meat, production technology, quality attribute, consumer acceptance

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Introduction

Cellular agriculture represents an emerging interdisciplinary field encompassing biotechnological applications involving cell cultures and tissue engineering (Choi et al., 2021). Its primary goal is to produce agricultural products without reliance on traditional animal farming, such as acellular (proteins, fat, additives, and

pigments) or cellular products (cell-based food and leather) (Lee et al., 2023). This innovative approach holds the potential to address the challenges posed by population growth, urbanization, and environmental degradation and pressing concerns like food security, which have become even more critical after the COVID-19 pandemic (Jairath et al., 2021). The escalating demand for meat protein, coupled with the limitations of resources such as land, water, and energy

required for conventional animal agriculture, underscores the urgency of exploring alternative solutions supposed to be more sustainable. Cellular agriculture is presented as one of them. Cell-based food (cultured meat in this review), the well-known example of cellular agriculture, has been under development for nearly 2 decades (Stephens et al., 2019). Throughout this period, it has exhibited continuous advancements in its journey toward replicating the authentic taste and texture of conventional meat while concurrently striving to decrease production costs to secure consumer acceptance. When it comes to environmental impact, studies are rare (Rodríguez Escobar et al., 2021), making it impossible to transparently verify the claims of companies in the sector. Thus, the techniques employed for cell-based food, primarily rooted in the medical area of cell culture and tissue engineering, necessitate further advancements. Consumer acceptance as a viable food source is also another question. In this review, we provide a comprehensive overview of the fundamental techniques underpinning cellular meat cultivation, drawing comparisons with their medical applications and conventional food sources. Also, we propose a research framework from the perspective of meat scientists aiming for the requisite similarities to conventional meat that cultured meat should exhibit, including a consideration of muscle maturation and essential sensory and

nutritional attributes, along with giving a review of current published research on consumer acceptance across different regions. Ultimately, we explore the possibility of integrating this technology into mainstream food consumption.

In Vitro Culture of Muscle

Cultured meat is theoretically produced through the following steps: (1) isolation of primary cells from animals or selection of cell lines, (2) sequential scale-up culture for mass production of cells, and (3) harvesting including differentiation into the desired tissue, as well as maturation of cells or processing the cells for use as food (Figure 1).

Different cell types for in vitro muscle culture

During embryonic development, skeletal muscles originate from the paraxial mesoderm through the differentiation of myogenic progenitor cells (Chal and Pourquié, 2017). These progenitor cells develop to muscle fibers and tissues through cell fusion events. Throughout an animal's entire lifespan, various types of stem cells, including embryonic stem cells (ESC), muscle stem cells (MuSC), and mesenchymal stem

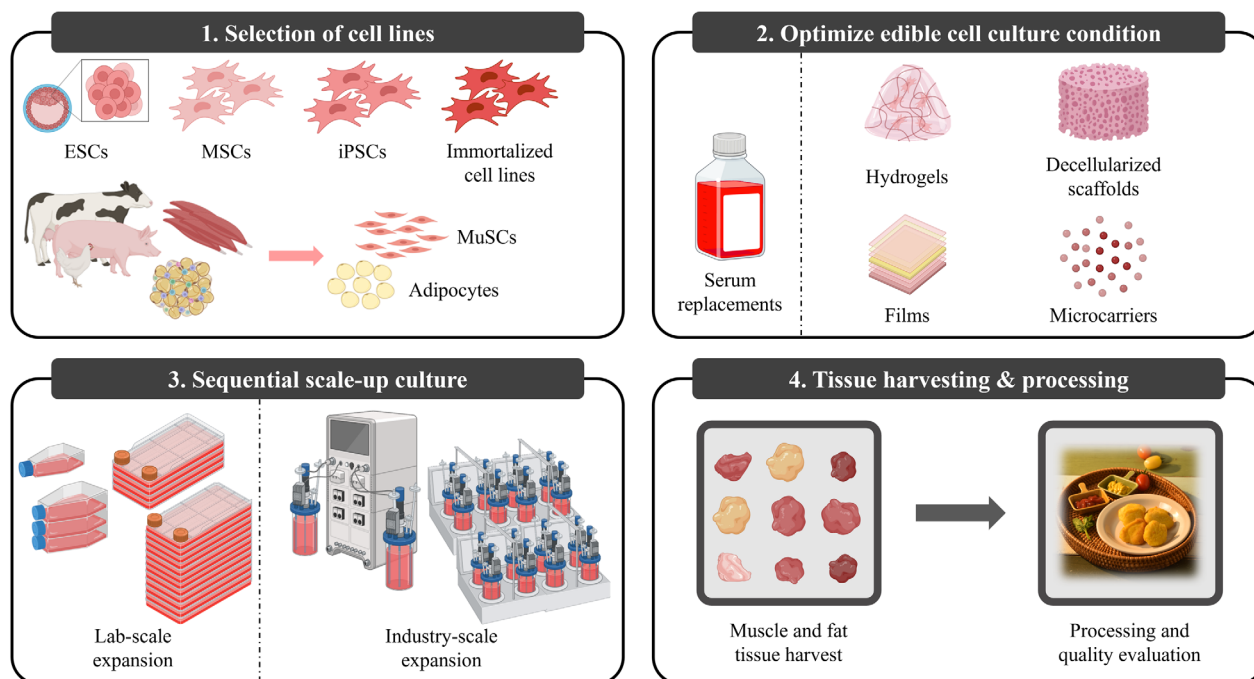


Figure 1. Key technological components vital for advancing cultured meat production. Cultured meat production integrates various technologies, with 4 key areas being critical: 1) cell type selection, involving embryonic stem cells (ESC), mesenchymal stem cells (MSC), induced pluripotent stem cells (iPSC), and muscle stem cells (MuSC); 2) edible cell culture condition adjustment through serum replacement and scaffold application; 3) culture scaling from laboratory to industrial scales; and 4) cultured tissue maturation and processing.

cells (MSC), contribute to muscle tissue generation (Chal and Pourquié, 2017). As a result, research focused on muscle tissue regeneration and growth draws extensively from studies involving these cell types. The production of cultured meat mirrors the principles of *in vivo* muscle regeneration. The theoretical framework and research underpinning cultured meat production also draw from these foundational studies on pluripotent stem cells (PSC), MSC, genetically modified cells such as induced pluripotent stem cells (iPSC), as well as MuSC.

ESC and iPSC

In theory, PSC represent an ideal cell source for cultured meat production as they eliminate the need for continuous animal sacrifice due to their indefinite “stemness,” a term that refers to the unique capacity of these cells for self-renewal and their potential to differentiate into a wide array of cell types (Choi et al., 2020). This characteristic of PSC allows for the sustained production of cellular material necessary for cultured meat, without resorting to the use of animals. Several studies have reported the establishment of ESC lines from both pigs and cows (Bogliotti et al., 2018; Choi et al., 2019). These ESC lines hold considerable potential for enhancing the efficiency of cultured meat production. In another way, researchers have explored the use of iPSC derived from domestic animals (Post et al., 2020). However, it is important to note that the generation of iPSC without transgene expression has not been reported to date. Moreover, the process of cellular reprogramming to create PSC from somatic cells raises concerns related to genetically modified organisms (GMO), which might be met with consumer resistance as GMO are not allowed in some countries such as in Europe (WHO, 2023). Furthermore, a notable limitation of PSC is the complex challenge of controlling their stemness *in vitro*, making the optimization process complex. Consequently, the commercialization of PSC as cell sources for the muscle culture may be a lengthy process.

MSC

MSC, primarily found in bone marrow, can also be present in various tissues such as skeletal muscle, umbilical cord, and adipose tissues, or acquired through differentiation from PSC *in vitro* culture. MSC are multipotent stem cells which could be differentiated into cells mesodermal-derived cells such as adipocytes, chondrocytes, and myogenic progenitor cells (Li et al., 2021b). Okamura et al. (2018) reported

that MSC derived from fetal bovine bone marrow exhibit myogenic potential, as evidenced by the expression of muscle regulatory factors. However, the formation of multinucleated muscle fibers was scarcely observed. Similarly, other studies have demonstrated the myogenic potential of human MSC derived from adipose tissue and synovial membrane (De Bari et al., 2003; Di Rocco et al., 2006; Stern-Straeter et al., 2014). MSC originate from different developmental pathways, with MuSC originating from the lateral-plate and paraxial mesoderm, respectively, therefore some studies have raised doubts about the myogenic capabilities of MSC (Leinroth et al., 2022; Uezumi et al., 2010). This debate raises concerns about the suitability of MSC for cultured muscle. However, it is worth noting that there have been studies suggesting that conditioned media from MSC culture can promote muscle regeneration (Archacka et al., 2021; Mitchell et al., 2019). Therefore, while MSC may not be ideal for direct muscle tissue culture, they could find application in co-culture systems or as a source of conditioned media for MuSC and adipose tissue culture.

Genetically modified cell lines

GMO have been a long-posed challenge to the consumer acceptance of novel foods developed through biotechnology. Recently, genetically modified pigs and salmon were approved by the US Food Drug Administration (FDA) as food (Dolgin, 2021; Waltz, 2017). In this regard, genetically modified cell lines also could be an option for cultured meat production except in the European Union. In fact, these types of cell lines were granted regulatory clearance by the US Food Drug Administration (FDA) and United States Department of Agriculture (USDA) in 2023 for the commercialization of cultured chicken meat (Zheng et al., 2024). Notably, this milestone was achieved through the use of both spontaneous and Telomerase Reverse Transcriptase-cisgenic immortalized chicken cell lines, as exemplified by companies such as Eat Just Inc. and Upside Foods Inc. (Azhar et al., 2023).

One of the potential genetic modification techniques of cells is transdifferentiation, a process involving the introduction of fully differentiated somatic cells to differentiate into other cell types through the ectopic expression of transcription factors. Jeong et al. (2021) succeeded the induction of fibroblasts, which can be more easily obtained from the animal body than MuSC and have the potential of transdifferentiation to muscle because of identical origin, to MuSC by reprogramming with MYOD1 overexpression.

Another genetic modification strategy is the process of immortalization. Senescence, loss of stemness in proliferation and differentiation, presents a significant challenge for MuSC when compared to other PSC, although it has a higher differentiation ratio to muscle than other cell types. Therefore, immortalizing primary cells holds an importance, as it directly influences production efficiency without necessitating the continual slaughtering of animals. Although naturally immortalized cell lines, such as C2C12—defined populations of cells that can be maintained in culture for an extended period of time, retaining stability of certain phenotypes and functions—are exceedingly challenging to obtain. In genetic engineering, telomerase (a telomere synthesis enzyme) along with BMI-1 and CDK4, which are cell cycle regulators, has been used to immortalize MuSC (Chua et al., 2019; Douillard-Guilloux et al., 2009; López et al., 2020).

The immortalized muscle cells can overcome the problem and provide uniform and consistent outputs. However, because the immortalized cells are programmed to possess excellent proliferation ability, the differentiation ability might be inferior to other cell types, which should be taken care of. Furthermore, genetic engineering techniques offer the possibility to modify genes such as myostatin, known for its role as a muscle growth inhibitor, with the aim of enhancing the productivity of cultured meat. This approach finds support in sheep research, where the knock-down of myostatin has been demonstrated to induce the proliferation and differentiation of sheep myoblasts, showcasing its potential for augmenting cultured meat production (Liu et al., 2012; Liu et al., 2014). Genetically modified cell lines have indefinite potential, while, as previously indicated, the issue of consumer acceptance remains a challenge.

MuSC

MuSC are muscle-resident stem cells including satellite cells or myoblasts located in the basal membrane of muscle fibers and capable of muscle fiber production. Because MuSC have more myogenic potential without genetic modification than other stem cell sources, these cells have been considered the first option for cultured meat production. Furthermore, many studies of isolation and culture condition for MuSC derived from livestock animals have been reported (Choi et al., 2021; Ryu et al., 2023). Therefore, many researchers and industries are using MuSC for cultured meat cell sources (Table 1).

The cell is a seed for cell-based food production. Nevertheless, it is regretful that many studies have used immortalized cell lines such as C2C12 derived from

Table 1. Cell lines and purification methods used in recent cell-based food research

Cell	Purification Method	Author/Year
C2C12	Commercial cell line	(Acevedo et al., 2018)
Rabbit skeletal muscle and bovine aortic smooth muscle cell	Commercial cell line	(MacQueen et al., 2019)
Bovine satellite cell, bovine smooth muscle cell, bovine endothelial cell	Pre-plating for satellite cell, others are commercial cell line	(Ben-Arye et al., 2020)
Bovine satellite cell, C2C12	Pre-plating for satellite cell and commercial cell line	(Stout et al., 2020)
Bovine satellite cell	-	(Furuhashi et al., 2021)
C2C12	Commercial cell line	(Jaques et al., 2021)
Bovine satellite cell	Pre-plating	(Jones et al., 2021)
Bovine satellite cell and bovine adipose-derived stem cell	FACS (CD31 ⁻ /CD45 ⁻ /CD56 ⁺ /CD29 ⁺)	(Kang et al., 2021)
Porcine satellite cell	-	(Li et al., 2021a)
Bovine satellite cell	FACS (CD29 ⁺ , CD44 ⁺ , CD344 ⁺)	(Naraoka et al., 2021)
C2C12	Commercial cell line	(Park et al., 2021b)
C2C12	Commercial cell line	(Park et al., 2021a)
Bovine satellite cell	-	(Skrivergaard et al., 2021)
Smooth muscle cell	-	(Zheng et al., 2021)
Bovine satellite cell	Pre-plating	(Andreassen et al., 2022)
Bovine fibro-adipogenic progenitor cells and satellite cell	FACS (CD29 ⁺ /CD56 ⁻ for fibro-adipogenic cells and CD29 ⁺ CD56 ⁺ for satellite cell)	(Andreassen et al., 2022; Dohmen et al., 2022)
Bovine satellite cell	-	(Dutta et al., 2022)
Porcine satellite cell	FACS (CD31 ⁻ /CD45 ⁻ /CD56 ⁺ /CD29 ⁺)	(Fang et al., 2022)
Porcine satellite cell	FACS (CD31 ⁻ /CD45 ⁻ /CD56 ⁺ /CD29 ⁺)	(Guo et al., 2022)
C2C12, RL34 rat hepatocytes	Commercial cell line	(Haraguchi et al., 2022)
Bovine satellite cell	Pre-plating	(Ivanovici et al., 2022)
Bovine mesenchymal stem cell	Pre-plating	(Joo et al., 2022)
Chicken and bovine satellite cell	Pre-plating	(Joo et al., 2022)
C2C12	Commercial cell line	(Lee et al., 2022c)
Porcine satellite cell	FACS (CD31 ⁻ /CD45 ⁻ /CD56 ⁺ /CD29 ⁺)	(Lei et al., 2022)
Porcine satellite cell and C2C12	Pre-plating and commercial cell line	(Li et al., 2022a)
C2C12, 3T3-L1	Commercial cell line	(Li et al., 2022b)
Porcine satellite cells, C2C12, 3T3-L1	FACS (CD31 ⁻ /CD45 ⁻ /CD56 ⁺ /CD29 ⁺) and commercial cell line	(Liu et al., 2022)

Table 1. (Continued)

Cell	Purification Method	Author/Year
Bovine satellite cell	FACS (CD31 ⁻ CD45 ⁻ CD56 ⁺ CD29 ⁺)	(Messmer et al., 2022)
C2C12	Commercial cell line	(Norris et al., 2022)
Bovine satellite cell	Pre-plating	(Okamoto et al., 2022)
Primary embryonic chicken muscle precursors, primary chicken muscle fibroblasts, C2C12	Pre-plating and commercial cell line	(O'Neill et al., 2022)
Bovine satellite cell	FACS (CD31 ⁻ CD45 ⁻ CD56 ⁺ CD29 ⁺)	(Park et al., 2022)
C2C12 and 3T3-L1	Commercial cell line	(Shahin-Shamsabadi and Selvaganapathy, 2022)
Adipose-derived mesenchymal stem cell		(Song et al., 2022)
Bovine satellite cell	Pre-plating	(Stout et al., 2022)
Porcine satellite cell, C2C12	Commercial cell lines	(Su et al., 2023)
Bovine satellite cell	Pre-plating	(Takahashi et al., 2022)
Bovine satellite cell	-	(Tanaka et al., 2022)
Bovine satellite cell	-	(Thyden et al., 2022)
Bovine satellite cell, 3T3	-	(Venkatesan et al., 2022)
C2C12	Commercial cell lines	(Wollschlaeger et al., 2022)
Bovine satellite cell, C2C12	Pre-plating and commercial cell line	(Xiang et al., 2022a)
Bovine satellite cell, C2C12	Pre-plating and commercial cell line	(Xiang et al., 2022b)
Mesenchymal stem cells		(Zagury et al., 2022)
C2C12, rabbit smooth muscle cell, sheep fibroblasts, bovine mesenchymal stem cells	-	(Zernov et al., 2022)
Smooth muscle cell		(Zheng et al., 2022a)
Smooth muscle cell		(Zheng et al., 2022b)
Porcine satellite cell	FACS (CD31 ⁻ /CD45 ⁻ /CD56 ⁺ /CD29 ⁺)	(Zhu et al., 2022)
Chicken embryonic fibroblast (spontaneous immortalized)		(Pasitka et al., 2023)
Bovine satellite cell	Pre-plating	(Stout et al., 2023b)
Immortalized bovine satellite cell	Pre-plating	(Stout et al., 2023a)
C2C12	Commercial cell line	(Wei et al., 2023)
Bovine satellite cell	Pre-plating	(Yamanaka et al., 2023)

FACS, fluorescence-activated single cell sorting.

mouse leg muscles. This is because they significantly differ from primary MuSC derived from domestic animals (Table 1). Consequently, the results obtained using the C2C12 cell line could not be directly applied to primary cells, and culture conditions suitable for primary cells need to be determined further, which is usually more difficult and tedious work to set up. For instance, optimizing the oxygen concentration, adjusting the serum composition in the growth medium, and calibrating the substrate stiffness are critical for enhancing the proliferation and differentiation of primary MuSC. Therefore, except for C2C12, notably, primary bovine and porcine MuSC have been the focus of extensive research, with the isolation of MuSC primarily achieved through techniques such as fluorescent-activated cell sorting (FACS) targeting both positive and negative markers such as Cluster of Differentiation (CD)31⁻CD45⁻CD56⁺CD29⁺ or pre-plating method. In the previous studies, the purity of MuSC was typically confirmed by the presence of markers such as PAX7⁺, MYOD⁺, CD29⁺ or CD56⁺ (Choi et al., 2020; Takahashi et al., 2022; Zhu et al., 2022). Consistent and reliable high production efficiency and product quality relies on the purity of MuSC, ensuring their purification from other cell types.

Some studies have explored genetically modified MuSC. For instance, Stout et al. (2020) demonstrated the development of carotenoid-producing bovine MuSC, and this research group subsequently published the findings on the immortalization of bovine MuSC through the overexpressing TERT and CDK4 genes (Stout et al., 2023a). In contrast, research involving other types of stem cells remains relatively limited, with only a few studies utilizing MSC for cultured fat production (Ivanovici et al., 2022; Song et al., 2022; Zagury et al., 2022; Zernov et al., 2022).

MuSC have emerged as the most successful cell type for cultured meat production to date due to their higher myogenic potential and their ability to directly contribute to muscle fiber formation without genetic modification.

Media components

Cell culture media significantly influences the determination of production costs, accounting for 55%–95% of the expenses and was a major factor behind the €250,000 (\$272,960) price tag of the first 142 g artificial hamburger in 2013 (Hubalek et al., 2022). For instance, it can be estimated that the production of 1000 kg of cultured meat requires approximately 10¹⁴ MuSC, which need 20,000 L of media

for their sustenance (Hubalek et al., 2022). These media typically comprise basal components, animal serums or substitutes, signaling molecules, and various additives crucial for optimal cell growth. Previous studies have comprehensively documented the components of these media (Choi et al., 2019; Lee et al., 2022a).

As mentioned earlier, the percentage of cell culture media in the production cost of cultured meat is very high. Accordingly, in order to reduce the production cost of cultured meat at a price acceptable to consumers, it is necessary to reduce the proportion of cell culture media. The first step of reducing cell culture media cost is serum replacement, especially fetal bovine serum. Serum consists of growth factors, hormones, amino acids, lipids, and unknown factors stimulating cell growth (Ho et al., 2021). Considering the limitations such as the unethical production process, batch-to-batch variation, animal origin, and high costs, serum replacement in cultured meat production is not only inevitable but essential. These challenges necessitate a holistic approach that encompasses scientific, economic, and social considerations. Scientifically, developing an effective serum replacement requires innovative research to identify alternatives that can support cellular growth and proliferation without compromising the quality of cultured meat. Economically, finding a cost-effective solution is crucial to making cultured meat affordable for consumers and viable for producers. Socially, addressing ethical concerns and public acceptance is key to integrating cultured meat into mainstream food systems. By incorporating these considerations, the pursuit of sustainable cultured meat production becomes a multidimensional effort to align technological advancements with broader societal goals. Therefore, some start-up companies seem to have taken some initiative and have recently succeeded in producing an artificial animal-free medium, but they are not disclosing its composition for reasons of industrial and commercial secrecy (Ho, 2021).

Indeed, FBS can potentially be substituted with protein hydrolysates derived from different protein-rich sources, including plants, fungi, and algae (Batish et al., 2022). An economical protein hydrolysate with potential to replace FBS An economical protein hydrolysate with potential to replace FBS has been obtained from the agro-industrial by-product okara (a byproduct of soymilk and tofu production) (Teng, 2022).

Nonetheless, it is noteworthy that the majority of recent studies have continued to rely on FBS or serum for cell proliferation and differentiation, as indicated in Table 2. In addition, cultured meat commercialized in

Singapore is produced using FBS (Zheng et al., 2024). Stout et al. (2022) developed chemically defined medium containing transforming growth factor, fibroblast growth factor, Neuregulin, transferrin, insulin, albumin, sodium selenite, and L-ascorbic acid 2-phosphate. This medium demonstrated equivalent or superior performance in the culture of bovine MuSC compared to media containing 20% FBS, while concurrently reducing the cost per liter by one-sixth compared to the later. Also, differentiation media which usually containing low concentration of serum than growth media could be replaced with chemically defined media (Messmer et al., 2022).

Another key area of research in cell culture media for cultured meat production involves substituting non-edible components with edible counterparts. For instance, certain non-edible ingredients traditionally used in culture media—such as synthetic growth factors, antibiotics, and other additives—can be replaced with edible alternatives, like plant extracts or food-grade growth factors. This substitution aims to enhance the safety and consumer acceptance of cultured meat while potentially reducing production costs. The related research is crucial for developing sustainable and economically viable cultured meat production. The supplementation of edible antioxidants such as vitamin C and flavonoids has demonstrated enhanced MuSC growth (Fang et al., 2022; Guo et al., 2022; Zhu et al., 2022). Furthermore, utilization of protein hydrolysates as serum replacement or media supplement also has been studied (Kim et al., 2023; Lei et al., 2022; Okamoto et al., 2022; Venkatesan et al., 2022). Nevertheless, it is important to note that even chemically defined media with serum replacements may still contain animal-origin components or costly ingredients, such as recombinant human albumin. A recent breakthrough by Stout et al. (2023b) involved substituting recombinant human albumin with hydrolysates derived from rapeseed.

Given that cell culture media significantly influences the cost and safety of cultured meat, the research and development aimed at cost reduction and defined components is an essential step toward the commercialization of cultured meat. A recent webinar by the Good Food Institute (Swartz, 2024) has described different possibilities to reduce costs of culture meat production considering growth media is the current cost driver while infrastructure will be a long-term cost driver. For example, sourcing lower-cost ingredients (by reducing pharma-grade ingredients or by using recombinant proteins) or reducing use or cost in production of growth factors has the potential to reduce media costs by 99%. Amino acids are also cost drivers and can be produced from hydrolysates to reduce their costs. Another

Table 2. Cell culture media for growth and differentiation and their supplements used in recent cultured meat research

Serum for growth media	Basal media for growth media	Supplements	Serum for differentiation media	Basal media for differentiation media	Supplements for differentiation media	Author/year
10% FBS	DMEM	L-glutamine	2% HS	DMEM		(Acevedo et al., 2018)
	Rabbit SkGMBovine SmGM					(MacQueen et al., 2019)
10% FBS	DMEM	ZnCl ₂ IGF, HB-EGF, FGF	2% HS	DMEM	IGF-1, HB-EGF	(Ben-Arye et al., 2020)
10% FBS for C2C12 20% FBS for bovine satellite cell	DMEM	FGF for bovine satellite cell	10% FBS for C2C12 20% FBS for bovine satellite cell	DMEM	FGF for bovine satellite cell	(Stout et al., 2020)
10% FBS	DMEM		2% HS	DMEM		(Furuhashi et al., 2021)
10% FBS	DMEM		-	-		(Jaques et al., 2021)
10% FBS	DMEM/F12	FGF, HGF, EGF, IGF	2% FBS	DMEM/F12	FGF, HGF, EGF, IGF	(Jones et al., 2021)
10% FBS for satellite cell 11%, 5%, 10% HS, 10% FBS, 10% HS 10% calf serum for ADSC	DMEM	FGF, p38 inhibitor	2% HS	DMEM		(Kang et al., 2021)
10% FBS	DMEM					(Li et al., 2021a)
20% FBS	DMEM	bFGF	5% HS	DMEM		(Naraoka et al., 2021)
5%, 10% FBS	DMEM	C-Phycocyanin				(Park et al., 2021b)
5%, 10% FBS	DMEM	C-Phycocyanin and IGF-1				(Park et al., 2021a)
10% FBS, 10% HS	DMEM	Sodium pyruvate	5% FBS	DMEM	Sodium pyruvate	(Skrivergaard et al., 2021)
20% FBS	DMEM/F12					(Zheng et al., 2021)
2% FBS, 2% Ultrosers G	DMEM					(Andreassen et al., 2022)
20% FBS	F10	FGF	2% FBS for satellite cell 1% FBS replacement for adipogenic cell	DMEM	Human insulin, rosiglitazone, IBMS, dexamethasone for adipogenic cell	(Dohmen et al., 2022)
5%, 10% FBS or 10% HS or 20% FBS+10% HS	DMEM	Soybean hydrolysates, cricket hydrolysates				(Dutta et al., 2022)
10% FBS	DMEM	Vitamin C	2% HS	DMEM	Vitamin C	(Fang et al., 2022)
20% FBS	F10	FGF, quercetin, icariin, 3,2'-dihydroxyflavone	2% HS	DMEM	Quercetin, icariin, 3,2'-dihydroxyflavone	(Guo et al., 2022)
Conditioned media from RL34 to C2C12	DMEM					(Haraguchi et al., 2022)
10% FBS	DMEM/F10	Non-essential amino acids, GlutaMAX, ZnCl ₂ , rHIGF, rhHB-EGF, bFGF	2% HS	DMEM	IGF-1, HB-EGF	(Janovici et al., 2022)

Table 2. (Continued)

Serum for growth media	Basal media for growth media	Supplements	Serum for differentiation media	Basal media for differentiation media	Supplements for differentiation media	Author/year
30% FBS	DMEM	GlutaMAX, bFGF	2% HS	DMEM		(Joo et al., 2022)
10% FBS	DMEM					(Lee et al., 2022c)
5% or 10% FBS	DMEM	FGF, IGF-1, PDGF-BB, EGF, LR3-IGF-1, VEGF, HGF, MGF, TGF- β , IFN- γ , IL-6, TNF- α	2% HS	DMEM		(Lei et al., 2022)
10% FBS for C2C12, 20% FBS for porcine satellite cell	DMEM/F12	FGF	2% HS	DMEM	FGF	(Li et al., 2022a)
10% FBS	DMEM		2% HS for C2C12 10% FBS for 3T3-L1	DMEM	Dexamethasone for C2C12 Insulin, dexamethasone, IBMX for 3T3	(Li et al., 2022b)
15% FBS for porcine satellite cell, 10% FBS for C2C12, 10% calf serum for 3T3	F10 for porcine satellite cell and DMEM for C2C12, 3T3	FGF	2% HS for muscle cells, 10% FBS for 3T3-L1	DMEM	Dexamethasone, IBMX, insulin for 3T3-L1	(Liu et al., 2022)
20% FBS for serum media or chemically defined FBS replacement for serum-free media	F10 for serum-containing media, DMEM/F12 for serum-free media	FGF for serum-containing media	2% FBS for serum-containing media	DMEM for serum-containing media, DMEM/F12 for serum-free media	EGF1, human serum albumin, vitamin C, MEM amino acids solution, insulin, LPA, transferrin	(Messmer et al., 2022)
10% FBS	DMEM		2% HS	DMEM		(Norris et al., 2022)
10% FBS	DMEM	Microalgae extracts	2% HS	DMEM	Microalgae extracts	(Okamoto et al., 2022)
20% FBS	DMEM/F10	FGF				(O'Neill et al., 2022)
20% FBS	F10		2% FBS	DMEM		(Park et al., 2022)
10% FBS	DMEM		2% HS for C2C12 10% FBS for 3T3-L1	DMEM	Insulin-transferrin-selenium for C2C12, Insulin, IBMX, dexamethasone, rosiglitazone for 3T3	(Shahin-Shamsabadi and Selvaganapathy, 2022)
10% FBS	DMEM/F12	FGF	10% FBS	DMEM/F12	Insulin, dexamethasone, IBMX, rosiglitazone	(Song et al., 2022)
Chemically defined serum replacement	DMEM/F12			Neurobasal/L15	IGF-1, EGF	(Stout et al., 2022)
10% FBS	DMEM	FGF for porcine satellite cell	10% FBS 2% HS for C2C12	DMEM	FGF for porcine satellite cell	(Su et al., 2023)
10% FBS	DMEM	FGF	2% HS	DMEM		(Takahashi et al., 2022)
10% FBS	DMEM	FGF				(Tanaka et al., 2022)
10% FBS	DMEM/F12	FGF, HGF, EGF, IGF				(Thyden et al., 2022)
10% FBS, 10% HS for bovine satellite cell 10% calf serum for 3T3	DMEM	Sodium pyruvate and recombinant GF produced by authors and commercial GF				(Venkatesan et al., 2022)
10% FBS	DMEM					(Wollschlaeger et al., 2022)

Table 2. (Continued)

Serum for growth media	Basal media for growth media	Supplements	Serum for differentiation media	Basal media for differentiation media	Supplements for differentiation media	Author/year
10% FBS for C2C12 20% FBS for bovine satellite cell	DMEM	FGF for bovine satellite cell	10% FBS for C2C12 20% FBS for bovine satellite cell	DMEM	FGF for bovine satellite cell	(Xiang et al., 2022a)
10% FBS for C2C12 20% FBS for bovine satellite cell	DMEM	FGF for bovine satellite cell	10% FBS for C2C12 20% FBS for bovine satellite cell	DMEM	FGF for bovine satellite cell	(Xiang et al., 2022b)
10% FBS	DMEM			DMEM	Rock-inhibitor, WNT inhibitor, FGF for differentiation Insulin, free fatty acids for maturation	(Zagury et al., 2022)
10% FCS	DMEM					(Zernov et al., 2022)
15% FBS	DMEM/F12	FGF	2% HS	DMEM/F12		(Zheng et al., 2022a)
15% FBS	DMEM/F12	FGF				(Zheng et al., 2022b)
20% FBS	F10	FGF, vitamin C	2% HS	DMEM		(Zhu et al., 2022)
10% FBS for serum-containing media	DMEM/DMEM/F12	Insulin, FGF, hydrocortisone, sodium selenite, L-alanine-L-glutamine, canola lipid mixture for serum-free media	10% FBS	DMEM	Oleic acid, rosiglitazone, pristanic acid, soy lecithin	(Pasitka et al., 2023)
Chemically defined serum replacement	DMEM/F12	Rapeseed protein isolates		Neurobasal/L15	IGF-1, EGF	(Stout et al., 2023b)
20% FBS	DMEM	FGF	2% FBS	DMEM		(Stout et al., 2023a)
10% FBS	DMEM		2% HS	DMEM		(Wei et al., 2023)
10% FBS or serum-free media Conditioned media from RL34 to C2C12	DMEM	Algae hydrolysates				(Yamanaka et al., 2023)

DMEM, dulbecco's modified eagle's medium; DMEM/F12, dulbecco's modified eagle medium/nutrient mixture F-12; FBS, fetal bovine serum; HS, horse serum; GF, growth factor; IGF, insulin like growth factor; rHIGF, recombinant human insulin-like growth factor; FGF, fibroblast growth factor; bFGF, basic fibroblast growth factor; EGF, epidermal growth factor; VEGF, vascular endothelial growth factor; HB-EGF, heparin-binding EGF-like growth factor; rhHB-EGF, recombinant human HB-EGF; PDGF-BB, platelet-derived growth factor-BB; HGF, hepatocyte growth factor; MGF, mechano growth factor; TGF- β , transforming growth factor-beta; ADSC, adipose-derived stem cell; IBMX, isobutylmethylxanthine; LPA, lysophosphatidic acid; IFN- γ , interferon gamma; IL-6, interleukin 6; TNF- α , tumor necrosis factor-alpha.

solution is media formulation optimization, media recycling, and the use of less media thanks to a better feed conversion of cells. Cell metabolism is indeed central to achieving goals of cost reduction.

In conclusion, while elimination of FBS in the culture medium is now a prerequisite, a significant reduction in the cost of culture media is needed to make their production economically viable since adding growth factors is expensive. Recycling of the culture medium, for example by recovering some of the residual nitrogen, is also a very promising way to

reduce the cost of its use and hence the price of the final product.

Scaffold

Scaffolds employed in *in vitro* cell culture aim to replicate the chemical, mechanical, and morphological characteristics of the extracellular matrix (ECM) found in living organisms (Samandari et al., 2023; Valdoz et al., 2021). In the field of tissue engineering, particularly for biomedical applications, a considerable effort

has been directed toward developing biomaterials, which can be broadly classified into 2 main categories: natural and synthetic (Seah et al., 2022). In muscle tissue engineering, there has been a historical preference for animal-derived biomaterials, mainly due to their accessibility and their inherent similarity to the native cellular microenvironment (Samandari et al., 2023). However, in cultured meat production, there exists consumer apprehension regarding the use of synthetic materials. Hence, recent research efforts in cultured meat have been directed toward the development of scaffolding materials that not only are edible and digestible but also align with consumer acceptability criteria including safety, taste, texture, nutritional value, ethical consideration, environmental impact, transparency, etc. These materials encompass plant-based, invertebrate-based, and microbial biomaterials (Ben-Arye et al., 2020; Jones et al., 2021; Park et al., 2021b).

While animal-derived biomaterials are not the preferred choice for cultured meat, a significant portion of current research has focused on previously developed biomaterials that include animal-derived components commonly used in biomedical applications, such as gelatin, fibrin, collagen, and Matrigel (MacQueen et al., 2019; Zhu et al., 2022). Despite their usefulness in other contexts, these animal-derived biomaterials conflict with their primary goal of producing alternative protein without animal slaughtering. They also suffer from issues like batch-to-batch variability, high production costs, and limited scalability. In this review, we classified scaffold structure as dried scaffolds, cell-laden hydrogels, films, and microcarriers (Table 3). Details on the characteristics, advantages, and disadvantages of each scaffold type can be found in previously published paper (Kumar et al., 2023). Ben-Arye et al. (2020) reported the soy protein-based edible scaffold for bovine MuSC, epithelial cells, and smooth muscle cells. The volunteers in this study evaluated the cultured meat product for its ability to generate flavor and texture of conventional meat after cooking. Following this study, researches on solid structure scaffolds mainly focused on edible materials from plants such as decellularized spinach, wheat glutenin, peanut or others (Ben-Arye et al., 2020; Ianovici et al., 2022; Jones et al., 2021; Song et al., 2022; Xiang et al., 2022b; Zheng et al., 2022b). Additionally, researchers also used edible yet non-plant-based sources for scaffolds such as chitosan, alginate, collagen, or gelatin (Lee et al., 2022c; Li et al., 2021a; Zheng et al., 2022a).

One of the prominent approaches of scaffold for cultured meat is hydrogel. While cells reside in pores of solid structure scaffold, hydrogel scaffolds involve

Table 3. Different scaffolds used for recent cultured meat research

Scaffold type	Materials	Author/year
Micropatterend film	Sodium alginate+agarose+fish gelatin	(Acevedo et al., 2018)
Dried scaffold	Crosslinked gelatin with mTG	(MacQueen et al., 2019)
Scaffold	Textured-soy protein based	(Ben-Arye et al., 2020)
Coated plate	Laminin	(Stout et al., 2020)
Cell laden hydrogel	Collagen or fibrin and Matrigel	(Furuhashi et al., 2021)
Micropatterend film	Sodium alginate+agarose+fish gelatin	(Jaques et al., 2021)
Decellularized plant	Decellularized spinach	(Jones et al., 2021)
Cell laden hydrogel	Collagen and fibrin	(Kang et al., 2021)
Cell laden hydrogel	Sodium alginate+porcine gelatin	(Li et al., 2021a)
Coated plate	Fibronectin	(Naraoka et al., 2021)
Film	Chitosan/cellulose with C-PC	(Park et al., 2021b)
Microsphere	Crosslinked gelatin with genipin, IGF-1, C-PC	(Park et al., 2021a)
Coated plate	Matrigel	(Skrivergaard et al., 2021)
Cell laden hydrogel	Collagen	(Zheng et al., 2021)
Microcarrier	Collagen, egg shell membrane or cytodex1	(Andreassen et al., 2022)
Cell laden hydrogel	Sodium alginate	(Andreassen et al., 2022; Dohmen et al., 2022)
Cell laden hydrogel	Sodium alginate, fish leatin with soybean and cricket hydrolysates	(Dutta et al., 2022)
Coated plate	Matrigel	(Fang et al., 2022)
Coated plate	Collagen	(Guo et al., 2022)
-	-	(Haraguchi et al., 2022)
Cell laden hydrogel	Aiginate-RGD with soy ptein isolate or pea protein isolate.	(Ianovici et al., 2022)
Coated plate	Gelatin	(Joo et al., 2022)
Dried scaffold	Dried textured vegetable proteins coated with fish gelatin and agar mixture	(Lee et al., 2022c)
Coated plate	Collagen	(Lei et al., 2022)
Dried scaffold	Sodium alginate+gelatin +collagen+chitosan	(Li et al., 2022a)
Micropatterned hydrogel	Porcine gelatin with soymilk	(Li et al., 2022b)
Microcarrier	Gelatin	(Liu et al., 2022)

Table 3. (Continued)

Scaffold type	Materials	Author/year
Cell laden hydrogel	Collagen+Matrigel	(Messmer et al., 2022)
Microcarrier	Crosslinked gelatin with mTG	(Norris et al., 2022)
Coated plate	Laminin	(Okamoto et al., 2022)
Coated plate	Matrigel	(O'Neill et al., 2022)
Coated plate	Collagen for proliferation test, Matrigel for differentiation test	(Park et al., 2022)
-	-	(Shahin-Shamsabadi and Selvaganapathy, 2022)
Dried scaffold	Peanut protein	(Song et al., 2022) (Stout et al., 2022)
Dried scaffold	Hordein, secalin, and zein	(Su et al., 2023)
Coated plate	Coated with fibronectin and cells were covered by fibrin+Matrigel hydrogel	(Takahashi et al., 2022)
Coated plate	Laminin	(Tanaka et al., 2022)
Decellularized plant	Decellularized broccoli	(Thyden et al., 2022)
Coated plate	Matrigel	(Venkatesan et al., 2022)
Cell laden hydrogel	Agar or XLB or gellan with pea and soy protein	(Wollschlaeger et al., 2022)
Film	Gelatin, soy, glutenin, zein, alginate, cellulose, konjac gum, chitosan	(Xiang et al., 2022a)
Dried scaffold	Glutenin	(Xiang et al., 2022b)
Cell laden hydrogel	Sodium alginate or collagen	(Zagury et al., 2022)
Microcarrier	Collagen and chitosan	(Zernov et al., 2022)
Dried scaffold	Peanut protein	(Zheng et al., 2022a)
Dried scaffold	Soybean, peanut, wheat	(Zheng et al., 2022b)
Cell laden hydrogel	Collagen and Matrigel	(Zhu et al., 2022)
Suspension culture		(Pasitka et al., 2023)
Coated plate	Laminin or fibronectin	(Stout et al., 2023b)
Coated plate	Laminin	(Stout et al., 2023a)
Dried scaffold	Soy protein	(Wei et al., 2023)
Culture plate	-	(Yamanaka et al., 2023)

mTG, microbial transglutaminase; IGF-1, insulin like growth factor 1; C-PC, C-phycoyanin.

mixing cells with the hydrogel, also called “cell laden.” This could achieve higher cell density than those of the solid scaffolds. Additionally, it can be used as a 3D printing bioink with cells inside. Furuhashi et al. (2021) showed their millimeter-thick bovine MuSC cultured steak with collagen hydrogel or fibrin-Matrigel hydrogel with an anchor mold system. Kang et al. (2021) used cell-laden hydrogel as a 3D bioink, enabling the creation of whole-cut meat-like tissues incorporating muscle, fat, and endothelial cells individually. In addition, alternative scaffolds such as films or microcarriers have been studied to facilitate the scalability and cost-effectiveness of cultured meat production (Park et al., 2021a; Park et al., 2021b; Thyden et al., 2022). The role of scaffolds in cultured meat production is important, impacting both the quality and cost of the final cultured meat products. Decellularized plant-based scaffolds, for example, can be used as a key component in affordable scale for cultured meat production system. Although recent scaffold research holds promise, the optimal strategies for cultured meat production remain to be definitely established.

In Vitro Culture of Fat

Fat significantly impacts the quality of meat, influencing taste, flavor, and tenderness, along with protein content (Clinquart et al., 2022). The amount and composition of fat and fatty acids in meat varies across species and breed within species, and is influenced by factors like age, diet, and environment (Fish et al., 2020). The nutritional value of fat in cultured meat is also one of the essential traits for consumer satisfaction. Even though some concerns have arisen regarding the health implications of excessive fat intake, recent studies have highlighted the significance of maintaining a balanced intake of fatty acids, with an emphasis on the ratio of saturated, monounsaturated, and polyunsaturated fatty acids, rather than fixing solely on overall fat quantity (ANSES, 2021; Laaksonen et al., 2005; Öhlund et al., 2008).

Therefore, the fat content in cultured meat is crucial in determining its nutritional value and sensory quality.

Adipogenesis process

Adipogenesis, the intricate process of fat cell development, entails the differentiation of multipotent MSC into adipocytes (Ali et al., 2013). This process involves 2 key stages: commitment to become

pre-adipocytes followed by subsequent terminal differentiation into mature adipocytes (Lee et al., 2023).

The induction of adipogenic differentiation relies on specific chemical compounds, while ongoing research endeavors aim to discover alternative methods for enhancing differentiation rates and prolonging adipocyte culture (Lefterova and Lazar, 2009). Precise manipulation of specific transcription factors guides MSC toward adipogenic differentiation. Within the stromal vascular fraction (SVF) of adipose tissue reside cells capable of differentiating into adipocytes, chondrocytes, and osteoblasts. However, challenges such as reduced differentiation potential with subculture and ethical concerns related to animal euthanasia limit the use of SVF-derived cells for *in vitro* culture of fat (Lee et al., 2023).

Researchers are focusing on establishing a stable and sustainable cell supply source for fat culture. Preadipocytes can be isolated from SVF cells using enzymes like collagenase. SVF comprises various cell types, including endothelial cells, pericytes, and macrophages (Guo et al., 2016). Ongoing research aims to classify pre-adipocytes, identifying cell lines with the highest potential for adipogenic differentiation. The isolation of pure preadipocytes significantly enhances their capacity to differentiate into mature adipocytes. Recent studies have explored co-culturing of adipocytes with muscle cells to supplement fat content, with a certain degree of success (Janovici et al., 2022; Song et al., 2022; Zagury et al., 2022).

Dedifferentiated fat (DFAT) cells have emerged as a potential alternative cell source for cultured fat production, given that SVF shows reduced adipogenic potential when cultured *in vitro* (Lee et al., 2023). DFAT cells are derived from fully mature adipocytes through a process known as ceiling culture, in which lipid storage in adipose cells decreases, leading to the cells reverting to fibroblast-like progenitor cells, known as DFAT cells. These cells possess the ability to differentiate into various mesenchymal lineages, including adipocytes and osteoblasts (Shen et al., 2011). Research has demonstrated that DFAT cells showed lipid accumulation per cell over extended culture periods (Yuen Jr et al., 2023). However, an inherent limitation of DFAT cells lies in their discrepancy on high serum concentrations, often ranging from 15% to 20%, for *in vitro* proliferation, the dependence on which raises concerns regarding cost and animal welfare implications, making it essential to develop serum-free culture conditions and address other characteristics of DFAT cell to facilitate their application in cultured fat production (Lee et al., 2023). A case study demonstrated the production of cultured meat with oleic acid

content similar to the one of the Wagyu cheek fat by adjusting the fatty acid composition of the culture medium (Louis et al., 2023).

Current studies and limitations

Compared to research on cultured muscle, there has been relatively less focus on cultured fat. Yuen Jr et al. (2023) recently introduced a method for producing bulk cell-cultured fat tissue, addressing challenges related to mass transport. They found this by initially culturing adipocytes in a 2D environment and subsequently aggregating them into 3D constructs. Another approach explored by researchers involved the use of adipose-derived stem cells on collagen-based 3D models to produce cultured fat. This method demonstrated texture and volatile compound similarities to animal-derived fat (Liu et al., 2023c). In a separate study, Song et al. (2022) focused on constructing cultured fat with porcine adipose-derived MSC on peanut wire-drawing protein scaffolds, showing promising potential for enhancing the quality of cultured meat. Furthermore, research involving bovine fat cells for cultured meat production has also been conducted, resulting in the creation of a fat-rich edible tissue with a marble-like structure that closely mimics the natural distribution of fat in meat (Zagury et al., 2022). Recently, Pasitka et al. (2023) demonstrated that spontaneously immortalized chicken embryo fibroblast could be good source of cultured fat. Their research revealed a high degree of differentiation into fat cells, as confirmed through both visual and sensory analysis. Collectively, these studies provide valuable insights and methodologies for the development of cultured fat, addressing both technological and sensory aspects. However, there is still progress to be made in fully replicating the characteristics of real animal fat tissues.

Muscle Maturity for Meat Similarity

Meat, traditionally defined as the flesh of an animal intended for human consumption, encompasses a wide range of edible components, including lean muscle, adipose tissue (fat), and various variety meats (Lee et al., 2020). Beyond its nutritional significance, meat plays a crucial role in human diet, culinary traditions, and social gatherings, holding cultural and sensory importance as a centerpiece (Hocquette, 2023).

Skeletal muscles in animals comprise approximately 90% muscle fibers and 10% other tissues, including connective tissue, fat, blood vessels, and nerve tissue

(Listrat et al., 2016). Tissue constituents collectively influence meat quality. Notably, muscle fiber types, classified as type I (slow-oxidative), type IIA (fast oxydolytic), type IIX, and type IIB (fast glycolytic), significantly impact meat characteristics (Joo et al., 2013). Type I muscle fibers are associated with red meat, higher myoglobin content, tenderness, juiciness, and distinctive flavor; fast-glycolytic fibers contribute to paler and less water-retentive meat (Lee et al., 2023) while fast-oxydolytic fibers contribute to tougher meat (Dransfield et al., 2003; Chriki et al., 2012). In the context of *in vitro* cultured muscle, it often consists of embryonic or neonatal muscle fibers, which may differ in maturity compared to muscle derived from live domestic animals (Thorrez and Vandenburg, 2019). Consequently, cultured meat may exhibit divergent sensory and processing characteristics compared to conventionally obtained meat (Fraeye et al., 2020).

A critical factor influencing meat quality is the sarcomere structure and its structural and functional proteins, including actin, desmin, filamin, myosin, nebulin, titin, and troponin-T (Lonergan et al., 2010). While *in vitro* cultured meat research typically focuses on aspects like contraction behavior and myosin expression, it rarely provides detailed insights into sarcomere structure of the muscle. This limitation may affect textural properties and overall meat quality due to the underdeveloped muscle structure and the lack of postmortem metabolism (Lee et al., 2023). Despite some studies reporting the development of steak-like cultured meat (Furuhashi et al., 2021; Kang et al., 2021), the prevalent immaturity of muscle structure and absence of fascia proteins often make cultured meat better suited for processed meat products. This immaturity arises from the differences between the natural muscle regeneration or development process in living organisms (*in vivo*) and the muscle cultivation process in controlled laboratory conditions (*in vitro*). In the *in vivo* state, muscle regeneration involves intricate interactions between various cell types, growth factors, and ECM components, leading to the formation of mature muscle tissue with well-defined structures, including fascia proteins. However, *in vitro* muscle culture lacks the dynamic environmental cues and complex interactions between and within organs and tissues which exist in living organisms, resulting in a less mature muscle structure. In this context, the expression of genes and the development of proteins associated with muscle ultrastructure and functions during an extended culture period should urgently be investigated. In addition, long-term culture optimization may serve as a viable approach for emulating the authentic *in vitro* formation of meat structure.

While meat traditionally serves as a significant source of essential nutrients, such as proteins, fats, micronutrients, and vitamins (Lee et al., 2020), information regarding the nutritional profile of cultured meat, the digestibility of nutrients and their absorption in the digestive tract of human beings remains limited (Fraeye et al., 2020). Cultured muscle cells are cultured within scaffolds, and the size of these scaffolds may surpass that of the muscle cells themselves, potentially resulting in lower nutritional density compared to conventional meat from livestock (Fraeye et al., 2020). Nutrient digestibility may also be affected by these changes in the muscle matrix (high scaffold volume). As previously indicated, fat also plays a vital role in determining the flavor, texture, nutrition, and visual appeal of meat. Despite advancements in meat analogues manufacturing processes, replicating the sensory properties of fat remains a challenge (Fish et al., 2020), especially because flavor is modulated in conventional meat by aging, a key process not studied so far in the cultured meat industry. Indeed, no study of the ageing phase in cultured meat has ever been published in a scientific article, and it is rarely mentioned by start-ups (Fraeye et al., 2020; Olenic and Thorrez, 2023; Wood et al., 2023).

A critical requirement for advancing the field of cultured meat is the establishment of a standard or grading system that assesses the maturity of the ultrastructure and its resemblance to meat sourced from livestock. Achieving a mature muscle structure through culture systems is crucial for mimicking real meat. Additionally, reproducing the aging process, which affects the sensory properties of conventional beef, is essential. However, it is still unknown how this will impact cultured meat. Moreover, the proportion of muscle and fat cells, reflecting the 80%–90% ratio found in traditional livestock meat, and the content of scaffolds in cultured meat are pivotal in defining or grading cultured meat. Ultimately, the overarching goal of cultured meat production is to develop a product fundamentally distinct from other meat analogues in meat similarity. According to survey research, consumers expect cultured meat to have a level of meat-like similarity that sets it apart from plant-based alternatives. To fulfil the consumer expectations and achieve market competitiveness, the culture of fat and other tissue components remains essential (Dueñas-Ocampo et al., 2023).

Cell-based Food Quality Evaluation

Quality assessment of food products, including meat, plays a pivotal role in providing objective

information regarding their characteristics. However, in the context of cell-based food products, the availability of scientific data pertaining to quality evaluation remains notably limited. This scarcity may be attributed, in part, to the high production costs associated with rigorous quality assessments and no wish from the private companies working in this area to communicate their results unlike academics. Recent studies have provided results of cultured meat quality through physicochemical analyses, sensory evaluations or both (Table 4).

Tenderness and texture are crucial indicators of meat quality, strongly influencing eating satisfaction. In Table 4, it is evident that a majority of studies have favored texture or rheological analysis over shear force measurements. While there were variations in experimental conditions across different studies, noteworthy and intriguing findings have emerged. Cultured meat from various cell sources has shown higher Young's modulus (Ben-Arye et al., 2020), compressive strength

(Lee et al., 2022c), Storage modulus (Liu et al., 2023c; Liu et al., 2022; Park et al., 2021a), and chewiness (Song et al., 2022) when compared to traditional meats such as bovine muscle, beef brisket or tenderloin, Shizitou (meat product), chicken breast, and porcine subcutaneous adipose tissue, respectively. However, some studies have reported lower hardness or rheological values than those found in conventional meat, and in some cases, no control group was included for comparison. As elucidated earlier, meat tenderness and texture are paramount for achieving eating satisfaction. Given the significant differences in experimental conditions for evaluating cultured meat in comparison to conventional meat, further research is essential to overcome these limitations and better emulate the characteristics of traditional meat.

Nutrition represents the foremost value of food and is the primary driver behind consumer consumption. Consequently, many previous studies in the field of cultured meat have assessed 'nutrition' from diverse

Table 4. Meat quality assessment in cultured meat research

Author/year	Quality items			Control compared with	Analysis tools
	Texture	Nutritional composition	Flavor		
(MacQueen et al., 2019)	○	-	-	Rabbit muscle, Beef tenderloin, Ground beef	Texture profile analysis
(Ben-Arye et al., 2020)	○	-	-	Native bovine muscle	Biodynamic test
(Furuhashi et al., 2021)	○	○	-	Beef tenderloin	Heating loss, breaking stress
(Park et al., 2021b)	-	-	-	-	Appearance
(Park et al., 2021a)	○	-	○	-	Storage modulus, appearance
(Zheng et al., 2021)	○	○	-	-	Pressure loss, total collagen content, texture profile analysis
(Andreassen et al., 2022; Dohmen et al., 2022)	-	○	○	Subcutaneous fat	Sensory analysis, lipidomic analysis
(Joo et al., 2022)	-	○	○	Chicken, cattle meat	Nucleotide-related compounds, amino acid composition, electronic tongue system
(Lee et al., 2022c)	○	-	○	Beef cuts of brisket, chuck, and tenderloin	Texture analyzer, flavor analysis
(Li et al., 2022a)	○	-	-	Pork	Texture analyzer
(Liu et al., 2022)	○	○	-	Commercial Shizitou	Storage modulus, loss modulus, nutritional evaluation
(Paredes et al., 2022)	○	-	-	Commercial processed Frankfurt-style sausages, processed turkey breast cold cut, non-processed raw breast chicken	Texture profile analysis, rheological characterization
(Shahin-Shamsabadi and Selvaganapathy, 2022)	-	○	-	-	Protein and lipid measurement
(Song et al., 2022)	○	○	-	Porcine subcutaneous adipose tissue	Texture profile analysis, GC-IMS analysis
(Su et al., 2023)	-	-	○	-	Appearances
(Tanaka et al., 2022)	○	○	-	Beef	Texture profile analysis, nutritional analysis
(Zagury et al., 2022)	○	-	-	-	Stiffness measurements, shrinkage measurements
(Zheng et al., 2022a)	○	-	○	Pork <i>longissimus dorsi</i> muscle	Texture profile analysis, sensory evaluation
(Zheng et al., 2022b)	○	○	-	Pork <i>longissimus dorsi</i> muscle	Texture profile analysis, total amino acids, SDS-PAGE, mass spectrometry analysis
(Zhu et al., 2022)	○	○	-	-	Tension testing, amino acid analysis
(Pasitka et al., 2023)	-	-	○	Chicken breast	Tasting

GC-IMS, Gas Chromatography - Ion Mobility Spectrometry; SDS-PAGE, sodium dodecyl sulfate - polyacrylamide gel electrophoresis.

perspectives, examining key components such as moisture, protein, and fat content. In terms of amino acid composition, significant disparities have been observed between cultured meats and their natural counterparts, with the exception of valine and tyrosine (Joo et al., 2022). Furthermore, investigations into fat content have revealed a shift in the fatty acid composition of bovine subcutaneous fat toward similarity with the late-stage culture, as opposed to the early stage (Dohmen et al., 2022). Notably, upon crafting meatballs using cell-based food produced with an ingredient list mirroring that of genuine products, it was evident that the protein content substantially exceeded that of commercially available counterparts, thus suggesting the potential for cultured meat to serve as a high-protein dietary option for consumers (Liu et al., 2022).

Flavor, encompassing attributes such as appearance, taste, and aroma, plays a pivotal role in consumers' food choices. Consequently, prior investigations into cultured meat have undertaken multifaceted evaluations of flavor. Similarity to conventional meat and consumer preference have been assessed using electronic tongue analysis, visual appearance evaluations, and sensory tastings. Cultured meat has been subjected to grilling or frying to assess its appearance, shape, and color (Park et al., 2021b), and pigments have been employed to replicate meat color (Park et al., 2021a; Su et al., 2023). It has been noted that the color of cultured fat tends to shift toward a more pronounced yellow hue with prolonged culture periods (Dohmen et al., 2022). Among the taste attributes of meat, umami taste is associated with nucleic acid compounds. Analysis of nucleic acid substances has revealed that cultured meat contains significantly lower levels compared to natural meat. Consequently, electronic tongue analyses have displayed discernible distinctions from conventional meat profiles (Joo et al., 2022). Sensory evaluations conducted through actual human consumption have supported these findings, indicating that the initial taste experience with cultured muscle tissue surpasses that of natural beef (Lee et al., 2022c). These results suggest that cultured meat offers an intriguing sensory experience to panelists in sensory tests and raises the possibility of cultured meat serving as a viable substitute for traditional meat (Pasitka et al., 2023).

Based on the research findings, cultured meat exhibits disparities when compared to conventional meat and meat products. Nevertheless, technological development progresses, and the enhancement of parameters encompassing texture, nutritional attributes, and sensory quality holds the potential to yield cultured meat that aligns with consumer expectations.

Commercialization Success and Weaknesses Around the World

The regulatory landscape for cultured meat has experienced significant advancements in various countries, suggesting a growing acceptance and integration into the global food system. Singapore led the charge in December 2020, becoming the first nation to approve the sale and consumption of cultured meat. Good Meat, a division of the US-based company Eat Just, received the inaugural regulatory approval to market its cultivated chicken, highlighting Singapore's forefront position in promoting cell-based meat innovations and initiating a worldwide regulatory shift toward more sustainable food sources (Food Ingredients First, 2023). Following in Singapore's footsteps, the United States made substantial regulatory progress. GOOD Meat and UPSIDE Foods were granted the FDA's "No Questions" letter, verifying their products' safety for consumer use (Webber, 2023). This approval initiated further examination by the USDA on labeling and facility inspections, leading to the novel assignment of inspectors to cultured meat facilities and establishing a commercial pathway for cultured meat in the US market. Concurrently, Israel achieved a significant milestone by allowing Aleph Farms to sell its cultivated beef, marking the first approval of its kind globally for cultured beef (Vegconomist, 2024). This approval not only positioned Israel as a leader in the Middle East but also as the third country worldwide to sanction cultured meat products, following Singapore and the US. The debut of Aleph Farms' premium Angus-style thin steak, named the Petit Steak, in select restaurants represented a major step toward the commercialization and wider acceptance of cultured meat products. Furthermore, start-ups worldwide are striving to secure governmental approvals, reflecting a robust and diverse effort to revolutionize the food industry with cultured meat solutions (Yun et al., 2024).

However, other voices are more critical or less enthusiastic (Hocquette et al., 2024). For instance, it has been speculated that the supply chain will suffer from power concentration and vertical concentration with only a few companies due to the huge investments required. The governance of the supply chain is also of great importance considering the risk of enhancing the disparity between Global North and South, the majority of start-up being in industrialized countries, and the main protein demand growth being in developing countries. The development of cultured meat may also result in high-price competitive meat with consequences for conventional livestock farming, such as its decline (with

the depression of rural economies) or its transformation into a premium market for specific consumer segments only (Mancini and Antonioli, 2022b). Alternatively, cultured meat may stay a niche market, which means that its expected benefits for consumers and the environment will not be reached in any case. More recently, a dozen European countries (including Italy, France, and Austria as leaders) and two American states (Alabama and Florida) expressed their wish to ban “cultured meat” (Hocquette et al., 2024).

Recent Consumer Acceptance of Cultured Meat

General observations

As with conventional meat (Liu et al., 2023b), consumer research on cultured meat suggests that several factors influence consumption decisions. These include cultural factors, such as different perceptions of “meat” in various countries, psychological factors such as safety concerns and food neophobia, and social factors, such as age, gender, education levels (Siddiqui et al., 2022), meat consumption levels, country of origin, or place of residence (Asioli et al., 2022; Kombolo Ngah et al., 2023; Liu et al., 2023a). The preference for cultured meat is commonly associated with its perceived societal, animal, and environmental potential benefits (Bekker et al., 2017). However, some consumers concerned for animal welfare and environmental issues may also not be convinced by the potential benefits of cultured meat for these issues (Hocquette et al., 2015; Liu et al., 2023a). On the other hand, many studies (Liu et al., 2021; Zhang et al., 2020) observed that the level of consumer education significantly increases the potential acceptance of cultured meat (Siddiqui et al., 2022). On the contrary, a better knowledge of the traditional meat sector significantly reduces the potential acceptance of cultured meat in China (Liu et al., 2021) as in other countries (Chriki et al., 2021; Hocquette et al., 2022; Jacobs et al., 2024; Liu et al., 2023a).

According to the literature, consumers who are skeptical about cultured meat are mainly concerned about the additives and chemicals that could be found in this new cellular food, but also about the possible long-term safety problems that could appear later on (Szejda and Dillard, 2020). Neophobic people, who are reluctant to test any new foods (Pliner and Hobden, 1992), are logically unlikely to accept cultured meat (Bryant et al., 2019; Hamlin et al., 2022; Siegrist and Hartmann, 2020). The most skeptical

generally reject cultured meat on moral (Schaefer and Savulescu, 2014) or religious grounds (Boereboom et al., 2022). A recent review showed that consumer acceptance/rejection of cultured meat also depends on public awareness in addition to perceived (un)naturalness and food-related risk perceptions related to uncertainties about the safety and health of cultured meat. Consumer acceptance/rejection of cultured meat also depends on the availability and potential benefits or quality attributes of other alternatives competing with cultured meat, such as plant-based meat substitutes (low price, low carbon footprint, taste, etc.) (Pakseresht et al., 2022). All these reasons support the idea that, in order to mitigate the doubts of some populations, the implementation of vigilant assessments of potential dangers and the development of effective communication are indispensable elements of the start-up strategy in favor of cultured meat.

So, in brief, positive attitudes toward cultured meat often align with concerns for human health, animal welfare, and environmental sustainability, while opposing viewpoints stem from factors such as disgust, negative beliefs about unnaturalness, and food neophobia (Weinrich et al., 2020).

Western perspective

Most studies related to consumer acceptance of cultured meat have been conducted in Western countries, especially in the US, The Netherlands, and the UK (Tsvakirai et al., 2024). Results have been previously reviewed (Ellies-Oury et al., 2022). On average, when different countries were compared, Spanish and French consumers are more reluctant compared to British consumers who exhibit a more positive attitude toward this new product (Siegrist and Hartmann, 2020; Asioli et al., 2022). French respondents expressed a higher level of disgust compared to British respondents, and French consumers also perceived cultured meat as less natural and more disgusting than consumers in any other country (Siegrist and Hartmann, 2020). Although potential acceptance of cultured meat is low in France—respondents were not familiar with “cultured meat”—young people and women are more in support of it due to a greater sensitivity to welfare and environmental issues associated to livestock (Hocquette et al., 2022). A low perception of conventional meat weaknesses, a low perception of cultured meat potential benefits, and/or a high perception of potential risks associated to cultured meat explain the potential low acceptance of cultured meat as in countries of South Europe. Indeed, many barriers not only

technological but also institutional and cultural have been identified for the acceptance of cultured meat in Italy (Mancini and Antonioli, 2022a). This may explain why Italy is the first country to want to ban cultured meat, arguing that the effects that the consumption of synthetic food could have on human health have not been verified at all, with possible negative effects (Hocquette et al., 2024). A similar law under examination has been proposed in France with the same objective to avoid any possible deterioration in human and animal health due to the consumption of cultured meat and also to protect the environment. In Spain, most of the respondents to a specific survey (Escribano et al., 2021) preferred to consume conventional meat produced through sustainable systems with information on the origin of meat products, rather than consuming meat alternatives including cultured meat. In Turkey, consumers do not consider cultured meat to be ethical, natural, healthy, tasty, or safe (Baybars et al., 2023). On the contrary, in the Northern Europe, such as Germany and Finland, cultured meat is perceived as a technocratic but a promising solution, as it can be an option for continued meat consumption without feelings of guilt associated with animal slaughter, but this requires guaranteed safety, affordable prices, and an authentic meat taste similar to or better than that of meat (Moritz et al., 2023).

Outside Europe, in line with a previous study (Siegrist and Hartmann, 2020), Australian respondents, especially those aged 35–54, were found to be significantly less willing to reduce their meat consumption and to consume meat alternatives including cultured meat compared to UK consumers (Ford et al., 2023). This may, at least, be explained by higher levels of meat consumption in Australia compared to the UK. In general, the highest levels of acceptance of cultured meat were observed in Mexico, South Africa, and England (Siegrist and Hartmann, 2020). So, South Africa is the African country with the highest level of potential acceptance of cultured meat (Kombolo Ngah et al., 2023). Familiarity with exotic or novel foods and influences from different countries, such as former colonies in the case of England or British culture in the case of South Africa, may explain why consumers of some countries such as the UK or South Africa are more receptive (Siegrist and Hartmann, 2020).

On average, and whichever the country, respondents who do not know the meat sector and who consume a low amount of meat and/or young or well-educated respondents (such as scientists) have the highest acceptance of cultured meat. On the opposite, people working within the meat sector or consuming more meat

have the lowest acceptance (Liu et al., 2021 and Liu et al., 2023c). In addition, an Irish survey showed that urban consumers were more receptive to cultured meat (Shaw and Mac Con Iomaire, 2019). Rural consumers were more concerned about the potentially negative effects that cultured meat production could have on agriculture and the farmers' lifestyles (Chriki et al., 2021; Dueñas-Ocampo et al., 2023).

Consequently, in countries such as Spain (Escribano et al., 2021), France (Hocquette et al., 2022), and Croatia (Faletar and Cerjak, 2022) as examples, different consumer segments can be identified according to consumers' moral and ethical concerns about livestock, about cultured meat, and about their perceptions of the impact of cultured meat production on the society and the economy.

Generally speaking, consumers express two broad categories of attitudes: (i) root attitudes, which arise from unconsciously elaborated behaviors with consumers' personalities, worldviews, culture, and motivations, (ii) surface attitudes that originate from consciously elaborated evaluations of product-specific attributes, and that explain why consumers' attitudes are malleable to change (Tsvakirai et al., 2024). Root attitudes are likely to explain why potential acceptance of cultured meat slightly differs between countries. In addition, consumers who expressed higher levels of trust in the stakeholders in the food domain perceived cultured meat as more natural than participants who had low levels of trust. Thus, trust was identified as a significant negative predictor of disgust evoked by cultured meat in Australia and the US but not in other Western countries (Siegrist and Hartmann, 2020).

Asian perspective

The global cultured meat market is expanding rapidly, with Asia emerging as a significant player in this field. In 2021, the investment in cultured meat in Asia reached \$62 million (USD) (Cohen et al., 2021), marking it as the fastest-growing area in the world's cultured meat market (Liang and Lee, 2022). Key contributors to this rapidly growing industry in Asia include Singapore, South Korea, China, and Japan. Notably, Singapore became the first country in the world to approve the commercial sale of cultured meat (Kantono et al., 2022). Given the active research and increasing investments in the remaining 3 countries—Korea, China, and Japan—where commercial approval is pending, it is imperative to gauge consumer awareness and acceptance to comprehend the rapid growth of the future Asian cultured meat market.

In China, a survey involving 1,019 adults to assess their willingness to purchase cultured meat found that 59.3% expressed a strong inclination to do so (Bryant et al., 2019), but this was not confirmed by a more recent study: Indeed, the answers of 4,666 respondents concluded that 19.9% and 9.6% of them were definitely willing to try and unwilling to try cultured meat, respectively, whereas 47.2% were not willing to eat it regularly, and 87.2% were willing to pay less for it compared to conventional meat. Finally, 52.9% of them will accept cultured meat as an alternative to conventional meat. Emotional resistance such as the perception of “absurdity or disgusting” would lead to no willingness to eat cultured meat regularly (Liu et al., 2021). Another study confirmed the high level of disgust expressed by Chinese consumers (Siegrist and Hartmann, 2020). The main concerns were related to safety and unnaturalness, but less to ethical and environmental issues as in Western countries. Nearly half of the respondents would like cultured meat to be safe, tasty, and nutritional. Although these expectations have low effects on willingness to try, they may induce consumers’ refusal to eat cultured meat regularly, underlying the weak relationship between wishes to try and to eat regularly (Liu et al., 2021).

In Japan, concerns about animal welfare and environmental issues positively correlate with the willingness to pay for cultured meat. However, social acceptance of cultured meat remains relatively low, standing at 40.9% (Takeda et al., 2023), mainly due to reservations about its perceived lack of naturalness. Interestingly, Japanese consumers are more inclined to experiment with cultured meat when in the company of friends, as opposed to family members (Motoki et al., 2022). These dynamics suggest that the acceptance of cultured meat in Japan may hinge on societal attitudes and contextual factors.

In Korea, an examination of cultured meat awareness revealed higher levels among men, younger individuals, those with higher educational attainment, and those with a greater interest in environmental issues (Lee et al., 2022b). Surveys conducted among Koreans of various ages and educational backgrounds unveiled mixed perceptions of cultured meat, shaped by sociocultural and demographic factors. Interestingly, 40%–80% of respondents expressed interest in purchasing cultured meat, with sustainability, food neophobia, and culinary curiosity identified as motivating factors for consumer acceptance (Hwang et al., 2020). On the other hand, based on the survey of consumer opinions on cultured meat conducted by Consumers Korea (2021), the following observations were made: 68.4% (342 individuals) expressed

agreement that cultured meat can help address food security issues and 51.6% (258) indicated agreement that cultured meat is necessary as an alternative to conventional meat for addressing food scarcity and environmental concerns. On the contrary, 39.4% disagreed that cultured meat is more beneficial for health, while 23.6% expressed agreement. Safety concerns were evident, with 38.0% considering it unsafe and 22.6% viewing it as safe.

In summary, assessments of cultured meat perceptions across 3 Asian countries indicate relatively lower consumer preference in Japan, while Korea and China demonstrate a higher degree of consumer acceptance. However, it is noteworthy that consumer perceptions of cultured meat exhibit notable similarities—motives and barriers for cultured meat acceptance—across these 3 countries as in other countries of the world.

Summary and Implications

Recent years have witnessed significant strides in the field of cultured meat, particularly in the areas of cell culture and tissue engineering. These advancements are pivotal in aligning cultured meat production with meat science principles, crucial for replicating the characteristics of real meat. The progress in this domain symbolizes a leap toward producing cultured meat that closely mirrors the sensory and physical attributes of traditional meat.

Despite these advancements, several challenges persist.

1. **Technical challenges:** Refinement of cell culture techniques and tissue engineering is ongoing. Achieving the precise texture and flavor of real meat remains a key obstacle.
2. **Consumer acceptance:** Ensuring sensory satisfaction is vital for widespread consumer acceptance. Current efforts are focused on making cultured meat indistinguishable from traditional meat to appeal to consumers.
3. **Quality aspect:** Addressing issues related to palatability and digestibility of nutrients is critical. The quality of cultured meat, in terms of taste and nutritional value, is under continuous assessment and improvement.
4. **Economic viability:** High production costs remain a significant hurdle. Cultured meat needs to be economically feasible for both producers and consumers to be a viable alternative to traditional meat.

5. Regulatory support: The regulatory landscape for cultured meat is still evolving. Ensuring compliance with food safety standards and acquiring necessary approvals are crucial steps for market entry.

In the short term, achieving the objectives of cultured meat production, including cost-effectiveness and consumer acceptance, appears challenging. However, with ongoing research and development in both public and private sectors, there is a potential for significant progress in the long term. These efforts are crucial for ensuring the feasibility and desirability of cultured meat as a sustainable and ethical alternative to traditional meat sources.

Conclusion

The journey toward realizing the full potential of cultured meat as a viable food source is complex and multifaceted. It requires a concerted effort from researchers, industry stakeholders, and legislators to overcome the technical, economic, social, and regulatory challenges. With continued innovation and public acceptance, cultured meat may become an integral part of our food system in the future. In this case, it should offer a sustainable and ethical solution to meet the growing global demand for meat.

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