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Review Article

Satellite Cell Biology and In Vitro Meat Production: From Muscle Stem Cell Niche to Commercial Scalability

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Abstract

Cultured meat — skeletal muscle tissue produced by the controlled proliferation and differentiation of muscle stem cells (satellite cells, SCs) outside the living animal — has transitioned from a speculative concept to a commercially approved food product within less than a decade, driven by growing global concern over the environmental sustainability, animal welfare implications, and pandemic risk potential of industrial livestock production. The first cultured beef burger, presented publicly by Mark Post in 2013, cost approximately €250,000 to produce; by 2020, cost estimates from commercial developers had fallen to the range of $10–50/kg, and Singapore had approved Eat Just's cultured chicken product for commercial sale. This review comprehensively examines the biology of satellite cells as the primary cellular substrate for cultured meat production, including their quiescent niche regulation, activation signalling cascades (HGF, FGF2, IGF-1, Notch/Wnt), in vitro proliferation kinetics, and differentiation into multinucleated myotubes. Critical process engineering challenges are systematically addressed: formulation of serum-free, food-safe culture media; scaffold materials enabling three-dimensional myotube organisation and maturation; bioreactor configurations suitable for scale-up to commercial production volumes; strategies for adipocyte integration to replicate the fat content of conventional meat; and the use of iPSC-derived myogenic cells to overcome the proliferative senescence of primary satellite cells. The review also addresses lifecycle assessment data comparing cultured meat's environmental footprint with conventional beef, pork, and chicken; regulatory approval pathways in the United States, European Union, and Singapore; and consumer acceptance research, with a particular focus on the factors that will determine the pace of mainstream market adoption.

Keywords: *Cultured meat, Satellite cells, Myogenesis, Serum-free media, Bioreactor scale-up, Scaffold, iPSC, Cellular agriculture, Food security, Environmental sustainability*

1. Introduction

The global food system is under mounting pressure from multiple converging crises. Livestock production accounts for approximately 14.5% of anthropogenic greenhouse gas (GHG) emissions (FAO, 2013), consumes ~77% of global agricultural land despite providing only 18% of global calorie supply (Poore & Nemecek, 2018), requires approximately 15,400 litres of water per kilogram of beef produced (Mekonnen & Hoekstra, 2012), and is the primary driver of tropical deforestation. It is simultaneously under existential threat from antimicrobial resistance — approximately 73% of global antibiotics are consumed by livestock — and from the pandemic risk posed by zoonotic pathogens emerging from intensive animal agriculture. These structural vulnerabilities have intensified interest in alternative protein production systems that decouple meat production from land use, water consumption, GHG emissions, and animal welfare concerns.

Cellular agriculture — the production of agricultural products directly from cell culture rather than from whole animals — offers a potential pathway to meat production with fundamentally different environmental and ethical characteristics. The concept was first articulated scientifically by Willem van Eelen, who filed the first cultured meat patent in 1999, and popularised by the work of NASA researchers investigating tissue engineering for long-duration spaceflight. The public debut of the first cultured beef burger at a press event in London on 5 August 2013, produced from bovine satellite cells expanded and differentiated in post's laboratory at Maastricht University at a cost of €250,000, marked the transition of the concept from theoretical speculation to laboratory reality (Post, 2012).

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The subsequent years saw extraordinary growth in commercial and academic interest. By 2020, over 80 companies globally were working on cultured meat, seafood, and fat products from cell culture. The most advanced — Eat Just (US), Mosa Meat (NL), Upside Foods (US), BlueNalu (US), and Shiok Meats (SG) — had progressed to pilot production facilities and were navigating regulatory approval processes. Singapore's December 2020 approval of Eat Just's cultured chicken nuggets under its Novel Food regulatory framework represented the first commercial authorisation of a cultured meat product anywhere in the world. The science underpinning these commercial developments — particularly the biology of satellite cells, the process engineering of large-scale cell culture, and the food science of cultured meat products — forms the subject of this review.

2. Satellite Cell Biology

2.1 The Satellite Cell Niche In Vivo

Satellite cells (SCs) are adult skeletal muscle stem cells resident in an anatomically defined niche between the plasma membrane (sarcolemma) and the outer basal lamina of individual muscle fibres. First identified by Alexander Mauro in 1961 using electron microscopy of frog muscle, SCs remained understudied for decades before molecular markers including Pax7 (paired box transcription factor 7), CD34, and syndecan-3/4 enabled their reliable identification, isolation, and characterisation. In adult skeletal muscle, the vast majority of SCs are quiescent — arrested in G0 phase — maintained in this state by a combination of extracellular matrix signals (Notch ligands Dll1/Dll4, Wnt inhibitors DKK1/SFRP3, Angiopoietin-1/Tie2 signalling), suppressive paracrine signals from adjacent muscle fibres (TGF-β, myostatin/MSTN), and intrinsic transcription factor regulation (Pax7+/MyoD$^-$ quiescent signature).

Upon muscle injury or experimental activation (mechanical perturbation, hepatocyte growth factor injection), quiescent SCs are released from niche constraints, re-enter the cell cycle, and undergo a characteristic sequence of molecular events: downregulation of Pax7, upregulation of Myf5 and MyoD (determination factors), rapid proliferative amplification over 3–5 days, and subsequent differentiation characterised by upregulation of myogenin and MRF4 (differentiation factors), cell cycle exit, and fusion into multinucleated myotubes. A subset of activated SCs returns to quiescence through asymmetric division and Pax7 re-expression, maintaining the SC pool for future regeneration rounds. This self-renewal capacity is essential for sustained cultured meat production, as it enables the generation of a theoretically unlimited number of myocytes from a single biopsy over many generations.

2.2 In Vitro Satellite Cell Expansion

For cultured meat, SCs are isolated from a small muscle biopsy (20–50 g from a live donor animal under local anaesthesia, without the need for slaughter) by enzymatic digestion (collagenase + dispase) followed by differential plating or fluorescence-activated cell sorting (FACS) using SC surface markers (SM/C-2.6 antibody for mouse, CD29+/CD56+/CD34$^+$ for bovine). Isolated SCs are seeded on tissue culture plastic coated with laminin, fibronectin, or Matrigel at optimal density (500–2,000 cells/cm^2) in a proliferation medium based on DMEM:F12 (3:1) supplemented with FGF2, HGF, and IGF-1. Under standard 20% O2/5% CO2 conditions, primary bovine SCs reach confluence in 3–5 days and can be passaged 15–30 times before entering replicative senescence and losing myogenic capacity. Reducing oxygen tension to 5% (physiological pO2) significantly extends the proliferative lifespan of primary SCs by reducing oxidative DNA damage and preserving telomere length.

3. Serum-Free Culture Media Development

Fetal bovine serum (FBS) has been the traditional culture medium supplement for mammalian cell culture since the 1950s, providing a complex and incompletely characterised mixture of growth factors, hormones, lipids, extracellular matrix proteins, and small molecules that collectively support cell adhesion, proliferation, and survival. FBS is included at 10–20% in standard SC growth media. However, FBS represents a critical barrier to cultured meat commercialisation for multiple reasons: it is expensive ($500–1,000/L, representing >90% of medium cost at research scale), subject to significant lot-to-lot variability, derived from bovine fetuses via a process with significant animal welfare concerns, and fundamentally inconsistent with the goal of animal-free meat production. Table 2 summarises the key growth factors present in FBS and their defined, recombinant replacements.

Table 2. Key growth factors in fetal bovine serum and their recombinant replacements for serum-free satellite cell culture media

Growth Factor	Target Receptor	Primary Function in SCs	Serum-free Replacement Strategy
FGF2 (bFGF)	FGFR1/2	Quiescent SC activation; proliferation	Recombinant FGF2 at 5–10 ng/mL; thermostabilised FGF2 variants
HGF	c-Met	Release from quiescence; chemotaxis	Recombinant HGF; NK1 fragment with preserved Met-binding

Growth Factor	Target Receptor	Primary Function in SCs	Serum-free Replacement Strategy
IGF-1	IGF-1R	Proliferation + differentiation (dual role)	Recombinant IGF-1 LR3 (long-acting); insulin at 1–10 µg/mL as partial substitute
EGF	EGFR	Proliferation; anti-apoptotic	Recombinant EGF at 10–20 ng/mL; combination with FGF2 synergistic
LIF	LIF-R/gp130	Self-renewal (context-dependent)	Recombinant LIF; role in bovine SCs under investigation
PDGF-BB	PDGFRβ	Fibroblast mitogen; SC crosstalk	Recombinant PDGF-BB; may improve co-culture myogenesis

FGF2 = Fibroblast growth factor 2; HGF = Hepatocyte growth factor; IGF-1 = Insulin-like growth factor 1; EGF = Epidermal growth factor; LIF = Leukaemia inhibitory factor; PDGF-BB = Platelet-derived growth factor BB; SC = Satellite cell.

Complete replacement of FBS with defined recombinant growth factor cocktails has been demonstrated for murine and human satellite/myoblast cells, but bovine SCs — the most relevant for beef cultured meat — remain more challenging due to species-specific growth factor requirements and the relatively limited commercial availability of bovine recombinant proteins. Plant-based protein hydrolysates (soy, wheat, rice) have been explored as low-cost bulk media supplements that provide amino acids, peptide growth factors, and micronutrients, with encouraging results in combination with minimal recombinant growth factor cocktails. Kolkmann et al. (2020) demonstrated a fully serum-free medium for bovine SC expansion that achieved comparable proliferation to FBS-supplemented control medium, representing an important milestone for the field.

4. Scaffolding and Three-Dimensional Structure

A key limitation of the first-generation cultured meat products was their thin, unstructured form factor — essentially a paste of myotubes pressed into a patty — which precluded replication of the texture, fibrous structure, and cross-sectional appearance of whole-cut meats such as steak or chicken breast. Generating structured 3D cultured meat requires the use of scaffolding materials that can support seeding, alignment, and maturation of myotubes in a three-dimensional geometry, ideally while being edible and food-safe. Table 3 summarises the major scaffolding materials investigated for cultured meat.

Table 3. Scaffolding materials investigated for three-dimensional structured cultured meat production

Scaffolding Material	Origin	Edible?	Key Properties and Limitations
Fibrin hydrogel	Bovine blood (thrombin + fibrinogen)	Yes	Biocompatible; supports myotube alignment; degraded by myotubes during culture
Alginate	Brown algae	Yes	Biocompatible; easy gelation; limited cell adhesion without RGD modification
Decellularised spinach leaf	Spinach (plant)	Yes	Intact vasculature topology; biocompatible; supports perfusion; structural
Decellularised apple hypanthium	Apple fruit	Yes	Open porous structure; cheap; supports 3D mammalian cell growth well
Electrospun gelatin/PCL fibres	Synthetic/animal derived	Partially	Controllable fibre alignment for muscle patterning; PCL not edible
3D bioprinted alginate/gelatin	Plant/animal derived	Yes	Customisable geometry; scalable; requires bioprinter investment

RGD = Arg-Gly-Asp integrin-binding peptide; PCL = Polycaprolactone; MSC = Mesenchymal stem cell.

Decellularised plant scaffolds have attracted considerable interest as a cheap, structurally complex, and naturally edible scaffolding platform. Modulevsky et al. (2014) demonstrated that the interconnected vascular network of decellularised apple hypanthium could support 3D mammalian cell growth, and subsequent work with decellularised spinach leaves showed that the intact vasculature topology — with channels as narrow as 10 µm — could support perfusion of nutrients deep into engineered tissue constructs, addressing one of the fundamental limits of diffusion-based nutrient supply in thick cultured meat. Food-grade decellularisation protocols using dilute SDS, enzymatic treatment, or high-pressure processing are being developed to remove cellular antigens while preserving structural integrity.

5. Bioreactor Scale-Up

The bioreactor represents the central process engineering challenge for commercially viable cultured meat. Laboratory-scale cultured meat production uses

standard tissue culture flasks and multi-layer cell factories, but commercial-scale production requires enclosed bioreactor systems operating under sterile, tightly controlled conditions at volumes orders of magnitude larger. Table 1 summarises current status and targets for the key engineering and commercial parameters.

Table 1. Key challenges and 2025 targets in cultured meat production technology

Challenge	Current Status (2020)	2025 Target	Primary Approach / Strategy
Serum-free media	Partial serum reduction to ~5%	Fully defined, serum-free	Recombinant GF cocktail (FGF2, HGF, IGF-1) + plant hydrolysates
Bioreactor scale-up	Stirred tank <100L scale	10,000L continuous perfusion	Microcarrier suspension + perfusion bioreactor + dissolved O2 control
Scaffolding for 3D structure	Fibrin/alginate 2D/thin sheets	Thick vascularised muscle tissue	Decellularised plant scaffolds; electrospun protein fibres; bioprinting
Adipocyte co-culture (fat)	Prototype co-culture feasibility	Marbled structured product	Induced adipogenesis from MSCs; fat layer co-deposition during culture
Senescence and cell line stability	Primary cells senescence at P30–35	Unlimited expansion via iPSC	iPSC-derived myogenic cells; immortalised primary satellite cell lines
Production cost (USD/kg)	~$10–50 (company estimates)	<$5/kg	Media cost reduction; bioreactor productivity; cell density maximisation
Consumer acceptance	Positive among early adopters	Mainstream acceptance	Price parity; transparent labelling; taste/texture equivalence to conventional

Microcarrier-based suspension bioreactors offer the most promising path to large-scale adherent cell culture, enabling high cell densities (>10^7 cells/mL) in standard stirred tank or rocking wave bioreactors with established scale-up characteristics from the biopharmaceutical industry. Edible microcarriers based on chitosan, zein, or textured soy protein would eliminate the need for microcarrier removal before consumption. Perfusion bioreactors — in which spent media is continuously exchanged while cells are retained — enable sustained high-density culture by preventing nutrient depletion and waste product accumulation, and are likely to be essential for the economic culture media utilisation that commercial production will require.

6. Environmental Impact and Sustainability

A central justification for cultured meat development is the potential for substantially lower environmental impact compared with conventional livestock production. Life cycle assessment (LCA) studies project that cultured beef produced at scale with renewable electricity could reduce GHG emissions by 78–96% relative to conventional beef, land use by 99%, and water use by 82–96% (Tuomisto et al., 2011; Mattick et al., 2015). However, Mattick et al. (2015) highlighted that the energy intensity of large-scale cell culture in controlled bioreactors could result in GHG emissions comparable to conventional poultry production when powered by fossil fuel electricity — emphasising that the sustainability of cultured meat is critically dependent on decarbonisation of the electricity supply.

The land use reduction potential is perhaps the most unambiguous environmental advantage of cultured meat. Cattle production requires approximately 164 m^2 of land per 100g of protein, compared with a theoretical requirement of <1 m^2 for cultured beef at scale, reflecting the dramatic increase in feed conversion efficiency when biological energy is directed entirely to target tissue production rather than to all other metabolic processes of a whole animal. This land use difference has enormous implications for biodiversity conservation, given that agricultural expansion is the leading driver of global habitat loss and species extinction.

7. Regulatory and Consumer Perspectives

The regulatory pathway for cultured meat differs fundamentally from that for novel plant-based proteins, as the production of edible tissue from mammalian cell culture represents a category of food with no direct regulatory precedent. Singapore's pioneering approval in December 2020 was preceded by extensive engagement between Eat Just and the Singapore Food Agency (SFA) under its novel food safety assessment framework, which evaluated cell line safety, culture medium composition, manufacturing process safety, and product nutritional equivalence with conventional chicken. The transparent, science-based approach adopted by the SFA has been widely praised as a model for other regulatory jurisdictions.

Consumer acceptance research consistently shows that younger, urban, and more environmentally and health-conscious consumers are most receptive to

cultured meat, with willingness to try exceeding 60–70% in many Western European and US surveys. The most frequently cited barriers to adoption are concern about safety/naturalness, price premium relative to conventional meat, and unfamiliarity with the production process. Price parity with conventional meat is identified as the single most important factor for mainstream adoption by the majority of surveyed consumers (Bryant & Barnett, 2018). The framing of cultured meat — whether as 'clean meat', 'lab-grown meat', 'cell-based meat', or 'cultivated meat' (the term now preferred by industry) — significantly affects consumer acceptance, with more neutral and scientifically accurate terms eliciting more positive responses.

8. Conclusions

Cultured meat has achieved in less than a decade what required half a century for in vitro fertilisation to accomplish: transition from laboratory demonstration to commercial regulatory approval. The foundational science — satellite cell biology, myogenic differentiation, tissue engineering, bioreactor design — is sufficiently mature to support continued rapid progress. The principal remaining barriers are economic (achieving cost parity with conventional meat), engineering (scaling serum-free production to commercial volumes and generating structured 3D products), and social (building consumer trust and regulatory acceptance globally). The convergence of cellular agriculture with advances in synthetic biology (engineered growth factors, biosensors for cell culture monitoring), biomaterials science (edible scaffolds), and process engineering (perfusion bioreactors) will define the pace at which these barriers are overcome. The implications for global food security, animal welfare, and environmental sustainability if cultured meat achieves mainstream adoption are profound — potentially representing the most consequential innovation in the history of animal biotechnology.

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