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Confluence of Cellular Agriculture: Clinical, Nutritional and Environmental Applications

By: Ella Maclear, Dylan Asunto, Sanjana Ramesh, Joseph Levin

Correspondence:
3lla@berkeley.edu

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Abstract

Cultured cells, grown from animal tissue in vitro, present a novel alternative to conventional meat production, with wide-ranging implications for regenerative medicine, nutrition, and environmental sustainability. On the clinical front, advances in cell culture techniques, scaffold engineering, and bioreactor technologies are cementing the role of cultured cells in regenerative medicine, creating new platforms for tissue repair and organ regeneration. Nutritionally, lab-grown meat can match the high protein content of traditional meat and improve digestibility and nutrient absorption, offering significant opportunities to enhance human health. Environmentally, it offers the potential to drastically reduce greenhouse gas emissions, land use, and water consumption compared to traditional livestock farming, while also mitigating the risk of numerous animal-borne diseases. This review synthesizes current literature on cultured meat, delineating its potential to transform food systems, public health, and biomedical innovation.

1. Introduction

Global meat consumption is projected to increase by over 70% by 2050, placing growing strain on environmental resources, food systems, and public health.[1] Diets high in processed and red meats have been linked to chronic conditions such as cardiovascular disease, type 2 diabetes, and certain cancers, contributing to rising healthcare burdens worldwide.[2,3] At the same time, an aging population and increasing prevalence of organ-damaging illnesses have exacerbated the shortage of transplantable organs. In the United States alone, more than 100,000 people are currently on the national transplant waiting list, with an average of 13 individuals dying each day without receiving a needed organ.[4] These converging crises highlight a dire need for innovative, cell-based solutions—both in the form of sustainable alternatives to conventional meat and in the advancement of regenerative medicine capable of growing functional tissues and organs in vitro. By bridging food science and biomedical innovation, cultured cell technologies hold immense potential to address both global food insecurity and the future of healthcare.

Cultured meat or clean meat is produced by isolating animal stem cells (typically muscle cells) and cultivating them in a nutrient-rich bioreactor and growing them on scaffolds that mimic the extracellular matrix.[5] These scaffolds replicate the structural and biochemical environment of native tissue, guiding the cells into forming organized, meat-like structures.[5] The transition from isolated animal stem cells to a consumable product is illustrated in ***Figure 1***.

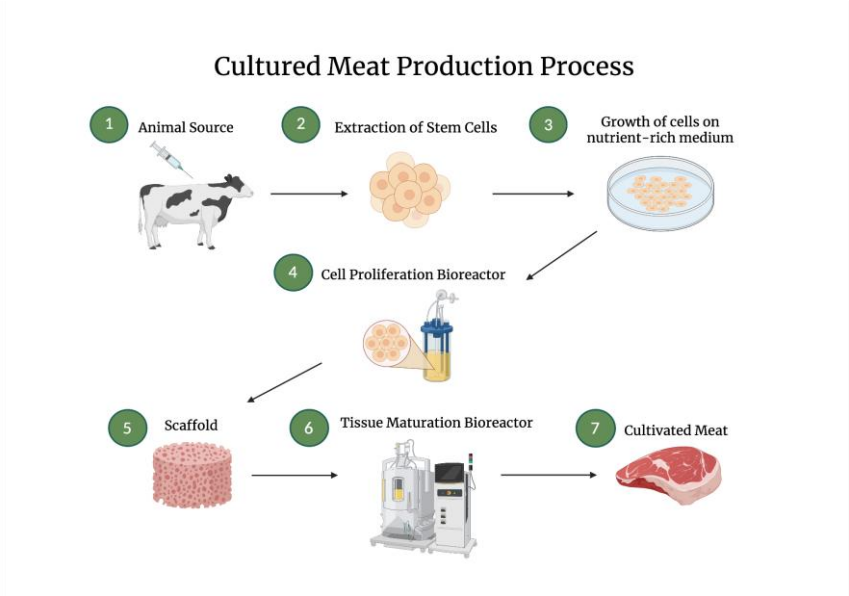

Figure 1: Cultured Meat Production Process

Starting with stem cells isolated from an animal source, cells are cultured in a nutrient-rich medium and expanded within bioreactors. The proliferating cells are seeded onto a biocompatible scaffold before undergoing maturation in tissue bioreactors. This process culminates in the formation of cultivated meat, ready for consumption.[5]

The idea of maintaining living cells outside the body dates back to the 1880s, when Wilhelm Roux maintained living chicken embryo cells in saline solution.[5] In 1990, Wilem van Eelen patented the industrial-scale production of meat from cultured cells (EP1037966B1), describing the use of large-scale bioreactors and non-toxic substances to grow lean, fat-free meat without bone or cartilage.[6] This patent laid the groundwork for modern cellular agriculture, enabling the cultivation of 3D meat tissues suitable for human consumption. A chronological overview of these milestones is presented in ***Figure 2***.

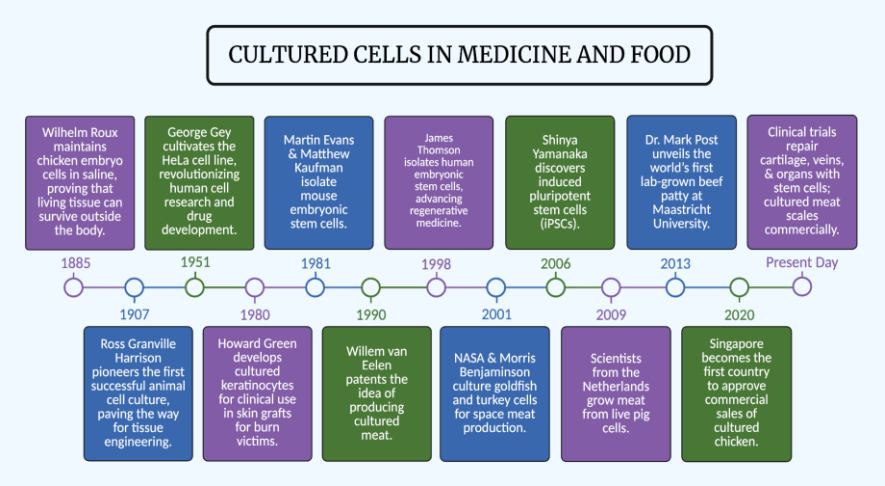

Figure 2: Timeline of Cultured Cells in Food and Medicine

A chronological overview of major scientific and commercial milestones in cultured cell technologies for food and medicine, spanning from early animal cell culture in the 1880s to present-day regenerative therapies and cultured meat commercialization.[5,7]

Since the early 2000s, research into cultured meat has rapidly accelerated and captured worldwide attention. One early sign of this growing interest was NASA's investigation into the feasibility of producing meat in space, aimed at providing sustainable nutrition for astronauts during long-duration mission.[5] A landmark moment came in 2013, when the world witnessed the unveiling of the first lab-grown beef patty by Dr. Mark Post, developed by researchers aiming to reduce the environmental impact and ethical concerns associated with conventional livestock farming.[5] More recently, Singapore became the first country to approve the commercial sale of cultured chicken, marking a major regulatory milestone and opening the door for broader market acceptance of lab-grown meat products.

In parallel, advances in cell culture and regenerative medicine have expanded the clinical relevance of cultured cells. The development of human embryonic stem (ES) cells and induced pluripotent stem cells (iPSCs) has enabled cell-based therapies for tissue repair and organ regeneration.[7] Innovations such as iPSC-derived dopaminergic neurons for Parkinson's disease and iPSC-derived retinal pigment

epithelial cells for macular degeneration demonstrate the potential of cultured stem cells to address complex diseases with precision and personalization.[7]

Despite their promising potential, cultured meat and regenerative cell technologies face significant challenges. High production costs, scalability issues, difficulties replicating the taste and texture of conventional meat, consumer skepticism, and complex regulatory landscapes remain key barriers.[8,9] In medicine, concerns around long-term efficacy, safety, and affordability are yet to be addressed.[8,9] In both domains, ongoing reliance on animal-derived inputs and energy-intensive processes further complicate large-scale adoption.

This paper explores the nutritional applications of lab-grown meat—including its potential to support individuals with specific macronutrient requirements, such as those with Glycogen Storage Disorder Type III—and examine its environmental promise in contrast to the zoonotic and ecological risks posed by traditional livestock farming. In this review, we investigate the evolution of cultured meat tissue from early breakthroughs to current advancements, assessing its potential on the cellular level to transform medicine, food production, and environmental sustainability.

2. Clinical Applications of Cultured Meat Technologies

The technologies underpinning cultured meat production are increasingly intersecting with the realm of clinical medicine, extending far beyond food production into therapeutic applications. The same fundamental tools used to develop edible muscle and fat tissues bioprinting, scaffold engineering, stem cell cultivation, and nutrient modulation are now enabling major advances in tissue grafting, regenerative therapies, and surgical reconstruction.[10] This convergence reflects a deeper biological truth: tissue engineering, whether for consumption or transplantation, must meet similar structural and functional criteria to successfully replicate the complexity of native biological systems.[10]

2.1 From Food Innovation to Functional Clinical Tissue

At the core of both cultured meat and regenerative medicine lies the challenge of creating living tissues outside the body that replicate native biological complexity. In food applications, this means mimicking texture, marbling, and nutritional density.[11] In clinical medicine, it means developing grafts or implants that can replace or regenerate damaged tissues, integrate seamlessly with the patient's body, and avoid immune rejection while maintaining long-term functionality.[11]

The overlap between these fields is exemplified by innovative scaffold materials. Decellularization, a process that removes all living cells from a biological tissue while leaving the structural scaffold intact, allows for the use of materials like mushroom scaffolds as a foundation for new cell growth. Decellularized mushroom scaffolds (DMS), originally explored as edible and biodegradable substrates in cultured meat production, demonstrate strong biocompatibility with human muscle cells, enabling early-stage differentiation and growth.[11] Their ability to provide supportive 3D structure without triggering adverse immune reactions positions them as ideal candidates for soft tissue grafts in clinical applications, offering both structural support and nutritional benefits when applied therapeutically.[11]

Fat tissue engineering represents another area of significant cross-sector innovation. Researchers have successfully created 3D bioprintable fat spheroids using bovine adipose stem cells structures originally designed to enhance texture and taste in cultured meat products.[12] These engineered fat tissues are now being investigated as customizable, metabolically stable fat grafts that could revolutionize reconstructive surgery by offering safer, more controllable alternatives to conventional fat transfer procedures, which often suffer from unpredictable resorption rates and donor site morbidity.[12] Additionally, recent studies have successfully sourced human adipogenic stem cells from endometrial tissue, providing another pathway for culturing personalized fat grafts with reduced rejection risk.[12]

The molecular-level parallels between food and clinical applications extend to functional optimization. In poultry studies, researchers demonstrated that dietary 25-hydroxycholecalciferol, an active form of vitamin D, stimulated breast muscle development via the mTOR pathway a key regulator of cell growth and regeneration in human tissues.[13] This finding suggests that by precisely engineering the nutritional environment of lab-grown tissues, scientists can tune not only their composition but also their regenerative potential, opening possibilities for designing tissues specifically tailored to particular healing outcomes and patient needs.[13]

2.2 Advanced Scaffold Design for Clinical Tissue Engineering

The integration of scaffold-based and scaffold-free approaches in cultured cell technology leverages advanced biomaterials, mechanobiology, and precision imaging to create sustainable, biocompatible tissue constructs with direct clinical applications[10], visualized in Figure 3. Edible scaffolds, including 3D porous structures, mats, and microcarriers made from gelatin, soy protein, or decellularized plant tissues such as celery and apple, are created using sophisticated techniques including 3D printing, extrusion, and decellularization protocols.[10]

Aleph Farms Ltd.'s innovative patent (US20240074456A1) exemplifies this advancement by combining plant-based or recombinant proteins with polysaccharides like alginate for 3D bioprinting of edible scaffolds.[10,14] These scaffolds not only support animal cell growth and mimic meat structure for food applications but also offer scalable, animal-free solutions with significant potential for clinical tissue grafts due to their customizable architecture and nutrient-perfused design.[10] The scaffolds are engineered to mimic the natural stiffness of muscle tissue (approximately 12–14 kPa), which promotes proper growth and development of muscle, fat, and blood vessel cells.[10] Their porous structure facilitates nutrient diffusion to reach thicker tissues, overcoming a critical limitation in tissue engineering applications.[10]

Silk fibroin scaffolds represent another breakthrough in biocompatible materials.[15] Produced using electrospinning techniques, these edible scaffolds yield nanofibers between 98 and 166 nanometers thick, supporting robust growth of bovine stem cells with the ability to expand cell populations ninefold within a week.[15] These scaffolds offer adjustable mechanical properties, though optimization for clinical applications may require blending with softer materials to better match the compliance of native muscle tissue and improve integration outcomes.[15]

Complementing scaffold-based approaches, scaffold-free technologies eliminate material frameworks entirely, employing advanced 3D bioprinting techniques including inkjet, micro-extrusion, and laser-based printing.[16] These methods utilize cell sheet technology with thermoresponsive poly(N-isopropylacrylamide) to create biomaterial-free tissues.[16] The approach leverages mechanosensing (the process by which cells detect and respond to mechanical stimuli in their environment) to trigger mesenchymal stem cell differentiation into specific lineages such as osteogenic or neural through integrin-dependent pathways.[16] High-resolution micro-CT imaging and sophisticated mathematical models like the Cellular Potts Model enable precise construct design and optimization.[16]

To address scalability challenges in clinical translation, automated systems such as Octane Biotech Inc.'s patented technology (US10844338B1) optimize tissue engineering through microprocessor-controlled monitoring of critical parameters including pH, temperature, and gas concentrations.[17] This technology supports multiple cell types on various scaffold platforms, offering applications spanning from cultured meat production to clinical tissue engineering, particularly for implantable grafts requiring precise environmental control.[17]

Understanding mechanical interactions between cells and their scaffolds remains critical for optimizing tissue development and clinical outcomes. The Rowat lab at UCLA has developed the parallel microfiltration (PMF) method, a high-throughput system designed to

measure cell deformability and stiffness—critical physical properties that influence cellular function and tissue integration.[18] While primarily applied to clinical fields such as cancer mechanobiology, where recent studies have examined beta-adrenergic signaling pathways and their effects on cancer cell stiffness and metastatic potential, these insights have broader relevance for tissue engineering applications.[18] The ability to measure and manipulate cell mechanical properties directly informs scaffold design optimization and tissue development protocols in both cultured meat and clinical applications.

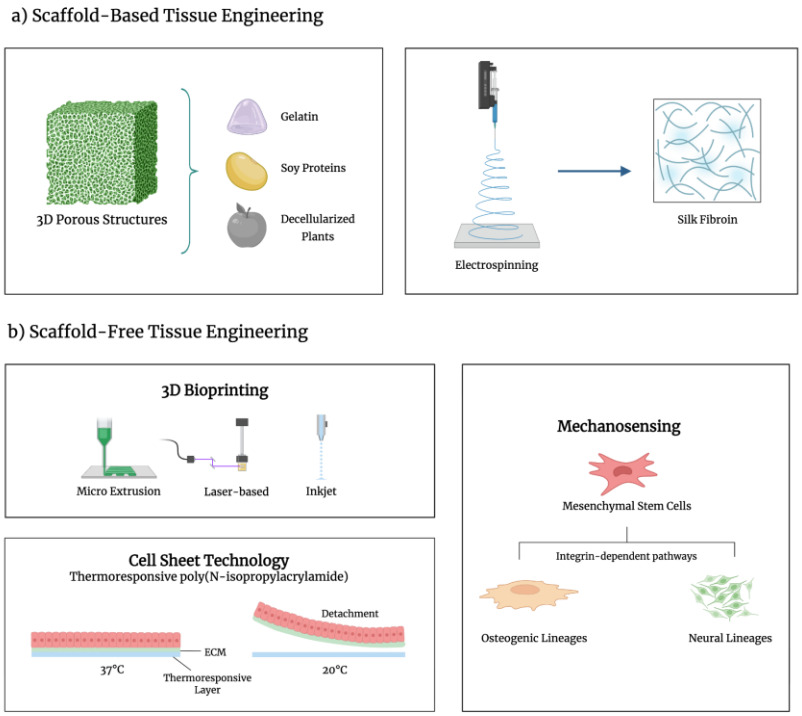

Figure 3: Comparison of Scaffold-Based vs. Scaffold-Free Tissue Engineering

a) Scaffold-based tissue engineering employs structured biomaterials to mimic the extracellular matrix, offering physical support for cell attachment, proliferation, and differentiation. Techniques such as electrospinning and 3D molding enable the fabrication of porous architectures from materials like gelatin, silk fibroin, or decellularized plant scaffolds.[15]

b) Scaffold-free strategies bypass the need for artificial frameworks, instead leveraging self-assembly, cell sheet engineering, and mechanobiological cues. Cells are encouraged to form tissues autonomously through methods like 3D bioprinting and thermoresponsive surfaces. These techniques aim to preserve native cell-cell and cell-matrix interactions while integrating mechanical signals to direct lineage specification. This paradigm supports the generation of tissues with minimal foreign material interference, enhancing translational potential.[15]

2.3 Precision Medicine Through Stem Cell Sorting and Characterization

Stem cell sorting techniques, refined through cultured meat development, are proving vital for clinical applications requiring precise cellular composition control.[7] In cultured meat production, scientists have developed sophisticated methods to selectively culture stem cells using specific surface markers, enabling the creation of structured tissues with controlled ratios of muscle and fat.[10], [12] This same precision can be leveraged in clinical settings to improve the consistency and safety of lab-grown grafts, particularly for complex reconstructive procedures requiring integration of multiple tissue types including muscle, connective tissue, and vascular components.[16], [17]

The precision achieved in cellular composition translates directly to predictable biological behavior after transplantation, a critical advantage over current autologous grafts, which often exhibit variable outcomes due to inherent biological heterogeneity.[11] Advanced cell sorting technologies enable clinicians to select optimal cell populations based on specific markers associated with regenerative potential, reducing the risk of treatment failure and improving long-term therapeutic outcomes.[7], [16]

2.4 Clinical Trials Demonstrating Cultured Cell Technology Translation

The convergence of cultured meat technology and clinical medicine is evident in numerous ongoing clinical trials that directly apply techniques and materials originally developed for food applications. These trials demonstrate the practical translation of tissue engineering innovations from laboratory to clinic, validating the therapeutic potential of cultured cell technologies.

A French clinical study is pioneering the engineering of functional bladder linings by culturing patient-derived urothelial cells on collagen and alginate scaffolds,[19] materials commonly employed in cultured meat production to recreate structured, functional tissues. These scaffolds support not only initial cell attachment but also long-term differentiation and survival under physiological stress conditions, critical requirements for any tissue substitute intended to withstand mechanical forces and maintain function in the harsh urinary environment.

Tissue-engineered vein replacement represents another compelling application, with clinical trials testing bioengineered grafts as replacements for malfunctioning valves in patients with chronic venous insufficiency.[20] These grafts are created through decellularization of donor veins followed by reseeding with the patient's own cells—a process nearly identical to decellularization and recellularization strategies employed in lab-grown meat production. The goal is creating functional, biocompatible vascular conduits that restore proper circulation without provoking immune rejection or thrombotic complications.

The CELLSPAN Esophageal Implant trial represents a particularly striking example of technology transfer,[21] utilizing cultured mesenchymal stem cells (MSCs) grown on synthetic scaffolds to rebuild damaged esophageal segments. The scaffold design governs both structural integrity and biological function, supporting cellular attachment, tissue regeneration, and mechanical stability functions

that directly mirror how meat production scaffolds maintain fat-muscle architecture and resilience under processing conditions.

Similarly, the ENCANTO trial is a randomized, controlled Phase II study investigating the therapeutic use of cultured cells in the treatment of patellofemoral osteoarthritis (PFOA).[22] Specifically, it utilizes nasal chondrocyte-based tissue engineered cartilage (N-TEC), created by expanding patient-derived nasal chondrocytes on a collagen type I/III scaffold.[22] These cultured cells generate cartilage-specific extracellular matrix over two weeks, forming a graft designed to restore damaged joint surfaces.[22] Originally inspired by scaffolding technologies used in cultured meat, the structural platform supports both cellular viability and mechanical resilience, making it suitable for load-bearing joints like the knee.[22] The study compares N-TEC to two standard-of-care interventions—Autologous Matrix Induced Chondrogenesis (AMIC) for early-stage PFOA and patellofemoral arthroplasty (PFA) for more advanced cases—across 150 patients in 11 clinical centers.[22] Beyond clinical outcomes, the trial evaluates N-TEC's regenerative potential through imaging-based assessments of joint structure and cartilage quality.[22] This exemplifies how cultured cell scaffolding technologies are being repurposed to support complex, load-bearing tissues in regenerative medicine.

In the field of ocular regeneration, the CECA trial investigates the therapeutic use of autologous limbal stem cells harvested from patients and cultured ex vivo to reconstruct damaged corneal epithelium in cases of limbal stem cell deficiency.[23] These patient-derived cells are expanded on collagen-based scaffolds to produce a functional epithelial graft that is surgically transplanted to restore the ocular surface.[23] This approach parallels scaffold-guided tissue engineering strategies employed in cultured meat, where biocompatible matrices support cellular growth and organization to recreate tissue architecture.[23] Currently in a combined Phase I/II design, the trial primarily assesses the safety and efficacy of this cultured cell graft in improving anatomical and functional outcomes, including corneal integrity and visual acuity, in affected patients.[23] This trial exemplifies the translational potential of cultured cell therapies and scaffold

technologies beyond food applications, extending into regenerative medicine for delicate, specialized tissues such as the cornea.

The FEMJA trial offers an alternative scaffold-free approach for treating bilateral total limbal stem cell deficiency by transplanting autologous oral mucosa epithelial sheets.[24] Instead of relying on an external scaffold, this method utilizes the natural cohesion of cultured epithelial cells to maintain tissue integrity.[24] These epithelial sheets are enzymatically detached using a collagenase-based process that preserves basement membrane proteins, allowing strong and rapid adhesion directly onto the corneal stroma without sutures.[24] This open-label Phase I/II trial, enrolling about 40 patients, evaluates the safety, tolerance, and efficacy of the graft by measuring improvements in visual acuity, corneal surface stability, neovascularization, and patient symptoms over a 24-month follow-up period.[24] The trial highlights innovative scaffoldless tissue engineering techniques that leverage cell-to-cell interactions to restore ocular surface function.

3. Advanced Therapeutic Applications and Future Directions

The clinical applications of cultured cell technology extend into highly specialized therapeutic areas, including adoptive cell transfer therapies and organ replacement strategies. Clinical trials such as the adoptive cell transfer of autologous tumor-infiltrating lymphocytes combined with high-dose interleukin-2 for solid tumor treatment demonstrate the sophisticated cellular manipulation techniques that share a common foundation with cultured meat research. These approaches require precise cell cultivation, expansion, and functional optimization; capabilities directly transferable from food production applications. This bidirectional exchange of innovation highlights how advancements in large-scale cell expansion, initially optimized for food production, can inform the precision required for specialized medical therapies.

One of the most compelling clinical promises of cultured tissue technology is the potential to eliminate or significantly reduce

dependence on donor grafts, whether from cadaveric sources or other anatomical sites within the patient's own body. Current reconstructive surgery often requires harvesting healthy tissue from one location (such as thigh muscle) to repair damage elsewhere (such as the calf), creating dual surgical trauma that increases recovery time, pain levels, and infection risk. Cultured grafts offer a transformative alternative: tissues grown to match the patient's specific immunological and anatomical profile, minimizing rejection risk while maximizing functional integration and therapeutic outcomes.

The clinical implications are profound and far-reaching. A patient undergoing facial reconstruction could receive precisely engineered grafts composed of lab-grown fat and muscle tissues tailored for both aesthetic integration and metabolic function. This approach would eliminate the need for additional surgical harvest sites, reduce hospital stays, minimize post-operative complications, and streamline recovery protocols while improving overall therapeutic outcomes.

3.1 Integration with Precision Medicine and Personalized Healthcare

The convergence of cultured cell technology with precision medicine represents a paradigm shift toward truly personalized healthcare. By combining patient-specific cell sources with engineered tissue scaffolds and controlled cultivation environments, clinicians can create therapeutic solutions tailored to individual genetic profiles, metabolic requirements, and healing capacities. This approach moves beyond the one-size-fits-all model of traditional medicine toward treatments designed and optimized for specific patients and clinical scenarios.

The integration of artificial intelligence and machine learning with cultured cell technology further enhances precision capabilities. Advanced algorithms can optimize cultivation parameters, predict tissue development outcomes, and customize scaffold designs based on patient-specific data including genetic markers, imaging studies, and clinical history. This convergence of biotechnology and computational

medicine promises to revolutionize therapeutic approaches across multiple medical specialties.

The technologies initially developed to replicate the taste, texture, and nutritional profile of conventional meat are now being deployed to heal human disease and restore physiological function. Whether through innovative scaffold design, nutrient-driven tissue growth, or stem cell precision techniques, the boundary between food science and regenerative medicine continues to dissolve. What was once considered speculative research is now being tested in hospitals and clinics worldwide, offering concrete evidence of a future where tissues are cultivated rather than harvested, and healing is designed from the cellular level upward.

This revolutionary approach to tissue engineering represents one of the most significant advances in modern medicine, with implications extending across surgical specialties, chronic disease management, and organ replacement therapies. As clinical trials continue to demonstrate safety and efficacy, cultured cell technology is positioned to transform healthcare delivery and patient outcomes on a global scale.

3.2 Nutritional Prospects of Lab Grown Meat

Recent developments in lab-grown meat suggest promising potential for improvements in consumers' fat and protein intake. Lab-grown meat greatly benefits consumers who require a specific level of fat or protein intake in their diet, such as individuals with glycogen storage disorder type III.

3.3 Glycogen Storage Disorder Type III

According to Andrea B Schreuder et al. in 2022, glycogen storage disorder type III (GSD III) is a metabolic condition that is passed down genetically through mutations in the AGL gene. As a result, the body is unable to obtain energy through glycogenolysis, referred to by Figure 4, and thus cannot rely on carbohydrates as a primary energy source. Instead, the body consumes lipids and protein for energy through ketosis and gluconeogenesis, respectively. This aligns with signs of hypoglycemia and elevated ketone concentrations in diagnosed

individuals.[25] GSD III also presents in multiple forms–primarily GSD IIIa and GSD IIIb. The former is the more common subtype and presents in about 85% of cases, with symptoms in the liver, skeletal muscle, and cardiac muscle. Meanwhile, the latter only presents in about 15% of cases, with patients exclusively facing liver complications.[26] Some cases have also shown digestive complications.[27]

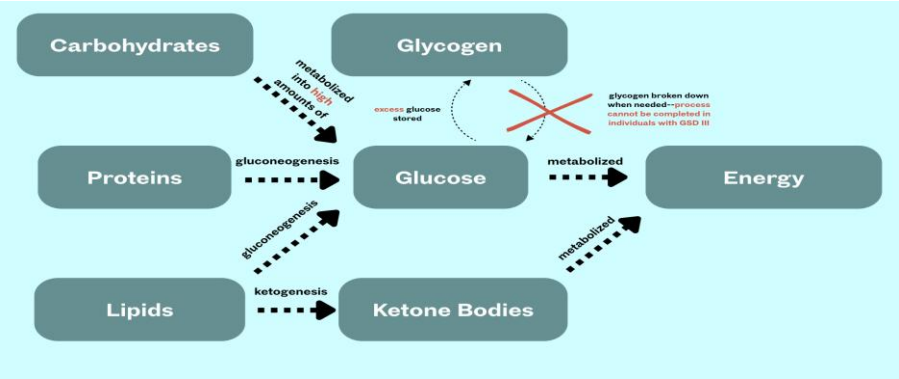

Figure 4: Relevant metabolic pathways for individuals with Glycogen Storage Disorder Type III.

Schematic describing the order of various metabolism pathways for energy in an individual affected by Glycogen Storage Disorder Type III (GSD III). Normally, humans metabolize food for energy through various pathways involving carbohydrates, proteins, and lipids, with the pathway from carbohydrates to glucose to energy being the main source. Excess glucose from both this pathway and gluconeogenesis (the synthesis of glucose from non-carbohydrate sources) are normally stored as glycogen and broken down by enzymes as needed. Patients with GSD III lack the enzymes for breaking down glycogen, making this storage pathway impractical. Thus, GSD III patients generally avoid the excess glucose produced from carbohydrate metabolism. More moderate amounts of glucose (such as those from gluconeogenesis) and energy from ketosis (metabolism of fats/lipids for energy) normalizes GSD III patients' energy levels while avoiding the glycogen breakdown pathway.

A study in 2011 suggests dietary management as an effective method to manage GSD III in everyday life. In the study, a two-month old infant facing hepatomegaly and cardiomyopathy from GSD IIIa was switched from a traditional high-carbohydrate diet to a low-carbohydrate, high-lipid, high-protein centered diet. It was hypothesized that the initial complications were due to glycogen

accumulation from the patient's diet prior to the experiment. For the first six months of the treatment, a diet consisting of 65% lipids, 15% protein, and 20% carbohydrates was administered through a nasogastric tube to avoid hypoglycemia, then taken in orally from month seven onwards. The modified lipid intake primarily consisted of d,l-3-OH butyrate (3OHB), a synthetic ketone body used to boost ketosis. Meanwhile, the modified protein intake aimed to increase gluconeogenesis. After recurring measurements over two years, the patient's cardiomyopathy improved (ventricular wall decreased in width) and liver growth stabilized. Additionally, the patient experienced no skeletal myopathy after becoming active. All these findings suggest an improved metabolism from a high-lipid, high-protein diet, which lab-grown meat could easily be customized to fit.[28]

3.4 Co-Cultivation of Muscle and Fat

During the cultivation process, lab-grown meat producers have full control of the lean meat and fat yield of the overall sample. In other words, the nature of the production process allows for customization of the resulting meat product's fat and protein content. This customization is mainly accomplished by raising muscle and fat cells in parallel through a process called in vitro co-cultivation, shown in Figure 5, which was tested by Yafang Wang et al. in 2022. Initially, myoblasts, the precursor cells for lean muscle tissue, are cultivated for proliferation in myocyte growth medium (M-GM), then mature and differentiate into myocytes in myocyte differentiation medium (M-DM). Meanwhile, adipocytes, the precursor cells for fatty tissue, are cultivated separately in adipocyte growth medium (F-GM), then mature and differentiate in adipocyte differentiation medium (F-DM). Shortly after maturation, a set of mature myocytes and adipocytes are taken from their separate containers and brought together on the same scaffold, which is the surface a cultured meat sample is grown on. Then, by exposing the initial group of myocytes and adipocytes to various culturing mediums, the muscle cells develop into a consumable meat product. Adipocytes are developed first, with the first two applied culturing mediums being F-DM and adipocyte maintenance medium (F-MM). Afterwards, the myocytes are fully developed with

the addition of M-DM.[12] This co-culturing strategy builds on decades of research into how myoblasts and adipocytes develop both in vitro and in vivo.

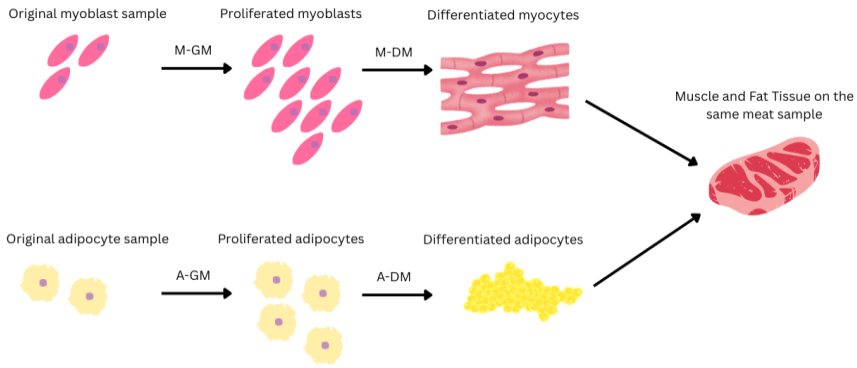

Figure 5: Parallel co-cultivation steps for biopsied myoblasts and adipocytes.

A visual depiction of the parallel pathways myoblast and adipocyte samples follow before their mature forms are combined to grow on the same cultivated meat sample.

In vivo, skeletal muscle development begins during embryogenesis, where paraxial mesodermal cells segment into somites—precursors to skeletal muscle. These somites respond to key signaling cues such as Wnt, FGF, BMP, and Shh, which activate transcription factors like Pax3, Myf5, MyoD, and myogenin, guiding the formation of multinucleated myofibers. Signaling from Myf5 and MyoD prompts these cells to proliferate until FGF is withdrawn, followed by myogenin expression to drive differentiation.[29] Adult muscle regeneration is driven by embryonic $Pax7^{+}$ satellite cells, which reside in a specialized niche and are activated in response to injury or stress.[30] The native environment also provides complex mechanical and systemic cues, such as hormones and immune factors, that tightly regulate tissue maintenance—factors often missing in lab-grown systems. In vitro, researchers aim to replicate these pathways using more controlled biochemical conditions. Vascular endothelial growth factor B (VEGFB) has emerged as a key regulator of myoblast proliferation and differentiation through the VEGFR1–

PI3K/Akt/mTOR signaling axis.[31] Other studies also suggest plasma as a potential booster to animal cell proliferation.[32] Moreover, pluripotent stem cells (PSCs) can be directed toward a muscle lineage by first exposing them to transcription factors MyoD and Pax3/7, which converts them to a myogenic cell intermediate. Then, by activating Wnt signaling and inhibiting BMP, these myogenic intermediate cells proliferate and differentiate into skeletal muscle tissue.[19] Differentiation may also be accelerated by inhibiting the expression of proliferation genes.[33] Despite these advances, most in vitro models fall short in mimicking full fiber maturation or recreating the satellite cell niche, which limits their regenerative fidelity.

In vivo, white adipocytes arise from mesenchymal stem-like progenitors within adipose tissue. These progenitors, identified by markers such as $CD29^+$, $CD34^+$, $Sca\text{-}1^+$, and $CD24^+$, differentiate under the control of transcription factors like PPARγ and C/EBPα, which initiate lipid accumulation and the formation of unilocular fat depots.[34] Importantly, this process occurs in close association with vascular networks, highlighting the importance of nutrient delivery and signaling crosstalk in adipose tissue development. In vitro, adipocytes are typically derived from mesenchymal stromal cells (MSCs) or preadipocyte lines using a standard cocktail of inducers like insulin, dexamethasone, IBMX, and indomethacin.[35] These activate adipogenic transcription factors and promote lipid droplet formation. However, 2D cultures often produce multilocular droplets, unlike the more physiologically relevant unilocular structure seen in vivo. Therefore, researchers have turned to 3D systems such as adipose spheroids and hyaluronic acid scaffolds, which better replicate the cell–matrix interactions and improve lipid accumulation and gene expression. There are also decellularized mushroom scaffolds, which exhibit high cytocompatibility with growing muscle tissue and provide essential nutrients when consumed.[36]

3.5 Transdifferentiation

A groundbreaking direction in cultured meat research focuses on converting myoblasts directly into adipocytes through transdifferentiation, visualized by Figure 6. In this process, a fully

differentiated muscle precursor adopts an adipogenic identity without reverting to a stem cell state. This switch is driven by transcriptional reprogramming: PPARγ and C/EBPα suppress myogenic factors like MyoD and myogenin, while activating adipogenic genes such as LPL and aP2.[37] Chemical inducers like all-trans retinoic acid (atRA) can accelerate this conversion via retinoic acid receptor pathways, and emerging evidence suggests that this effect is direct and not dependent on protein synthesis.[38] Physiological stressors such as oxidative damage, aging, and muscle injury also promote this switch through pathways like Wnt/β-catenin and NF-κB/YY1. Moreover, microRNAs—including miR-133, miR-193b/365, and miR-206—fine-tune the balance between myogenic and adipogenic programs.[39] In cultured meat applications, this plasticity enables the production of both muscle and fat from a single progenitor source, streamlining manufacturing and enhancing qualities like marbling and flavor.

Transdifferentiation of muscle cell precursors to fat cells also goes beyond white and red meat, opening potential avenues in cultivating seafood. In a study by Haowen Yin et al. in 2025, the differences between traditional adipose stem cell differentiation and muscle stem cell transdifferentiation in yellow croaker tissues were assessed. In particular, the different levels in lipid metabolites between the two different cell types were compared. Traditionally differentiated adipocyte cells showed higher triacylglycerol levels, implying the tissue's high potency as an energy reserve. Meanwhile, transdifferentiated muscle stem cells showed higher levels of glycerophospholipids, which are valuable in signaling pathways regulating lipid synthesis and catabolism.[39] This study suggests that when cultivating fish meat, the resulting fat content can be customized to either provide greater amounts of energy or aid the consumer's lipid metabolism. Lipid metabolites are also essential for flavor, and the presence of lipid metabolites in transdifferentiated fat tissue demonstrates a potential method to modify cultured meat flavors. A deep level of flavor customization may be possible due to the slightly different ratios between lipid metabolites in traditional fat compared to transdifferentiated fat.[39] Additionally, the success of transdifferentiation in this study presents an alternative to co-

cultivation in meat cultivation, as it requires existing transcription factors instead of various mediums. However, further research is required to compare the two fat modification methods.

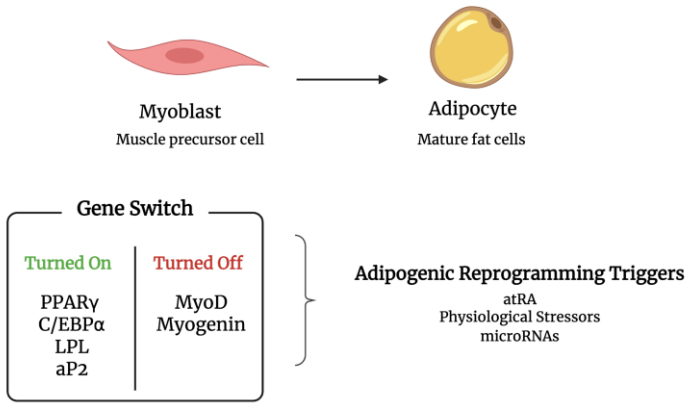

Figure 6: Transdifferentiation of Myoblasts to Adipocytes
Schematic depicting the direct transdifferentiation of muscle precursor cells (myoblasts) into mature fat cells (adipocytes) without reverting to a stem cell state. Key transcription factors PPARγ and C/EBPα suppress myogenic genes (MyoD, Myogenin) while activating adipogenic genes (LPL, aP2). Chemical inducers like all-trans retinoic acid (atRA), physiological stressors, and microRNAs coordinate to regulate this gene switch. This plasticity enables efficient generation of both muscle and fat cells from a single progenitor source.

3.6 Beyond Traditional Nutrition

While most current research aims to fine-tune the lab-grown meat production process such that it rivals traditional livestock meat production, recent studies show its potential as a superfood.[18] For example, a study in 2020 by Andrew Stout et al. showed that cultured mammalian cells can be genetically engineered to adopt plant nutrient synthesis pathways, all while maintaining normal levels of proliferation and differentiation.[40] Normally, animal sources of these plant nutrients remain unrecognized due to their low levels in traditional livestock.

Previous studies show a slight upward trend for phytonutrient levels in grass-fed livestock versus grain-fed livestock.[41, 42] However, by introducing bacterial amino acid sequences phytoene synthase (CrtB), phytoene desaturase (CrtI), and lycopene cyclase (CrtY) to mammalian muscle cells, the cultured animal tissues are able to convert an existing metabolite into the carotenoid phytonutrients phytoene, lycopene, and β-carotene, whose structures and compositions are provided in Figure 7. When fully optimized, these cells can produce phytonutrient levels over 14 times greater than traditional livestock.[40]

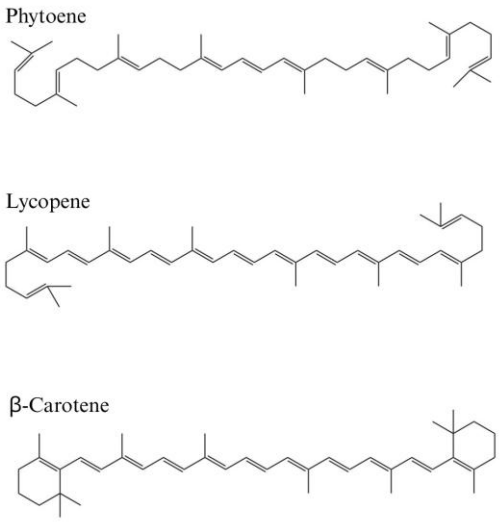

Figure 7: Phytoene, lycopene, and beta-carotene molecular structures.

A visualization of the structures and chemical compositions of the carotenoids produced in the cultivated meat samples from Stout's experiment. Their composition of alternating double bonds along a molecule consisting of only carbons and hydrogens helps aid their role in stabilizing stray molecules in the human body.

Despite their simple composition of carbons and hydrogens, these three carotenoid phytonutrients are vital in both nutrition and regenerative medicine.[43, 44] The colorless carotenoid phytoene acts as an antioxidant, contributes to anti-inflammatory responses, protects lymphocytes from DNA damage, and protects against light-induced cancers when applied topically.[45] More recent studies suggest that phytoene also has anti-aging properties, counteracting the effects of chronic age-related diseases such as Alzheimer's.[46] Phytoene serves as the precursor molecule to lycopene and beta-carotene.[45, 46] Studies

show correlations between the latter two carotenoids and a decreased risk for cardiovascular disease and cancers. [43, 44, 47]

4. Environment & Public Health Impacts, Risks of Current Livestock Meat Sources

4.1 Traditional Meat Production and its Environmental Impacts

Lab-grown meats can serve as a safer and healthier form of meat production for the society and environment. The current system for traditional meat production, agricultural livestock, is characteristically harmful to the environment in several ways, which can be represented in Figure 8. Namely, a 2017 study conducted by Michael Clark and David Tilman[48] found that, compared to the production of dairy and plant-based products, ruminant meat production emits significantly more greenhouse gases (20-25 g CO_2 equiv/kcal compared to 0-5 g), uses significantly more land and energy (0.075-0.125 m^2/kcal to 0-0.025, 20-30 kJ/kcal to 0-10), and has significant higher potential for acidification (the buildup of hydrogen ions that lowers the pH of the soil and water) and eutrophication (the over enrichment of water with nutrients, leading to harmful algal blooms and oxygen depletion that threatens aquatic life) (0.20-0.35 g SO_4/kcal to 0-0.05, 0.125-0.175 g PO_4/kcal to 0-0.025).[48] Livestock cattle also contribute to about 14.5% of all greenhouse gas emissions.[49] These parameters can lead to many environmental consequences, including deforestation, soil erosion, and water pollution.[50] Traditional meat production can negatively impact our environment, along with the welfare of several animal groups and their natural habitats.

4.2 Illnesses and Infectious Diseases Linked to Traditional Meat Production

Traditional meat production is also linked to many illnesses, including zoonotic diseases, which are diseases spread between animals and humans. Two-thirds of all the emerging infectious diseases in recent history derive from animals, and animal farms are hotspots for such.[51] For one, livestock farms create large amounts of particular matter and

ammonia, both of which have been known to harm adults and children that live in local residential areas, through conditions such as acute lung disorder and asthma.[52] Furthermore, endotoxin, a form of organic particulate matter emitted by livestock farms, can be spread throughout the air and can lead to bronchitis via airway inflammation.[43] Apart from these conditions, the World Health Organization has reported concerns regarding the over-usage of antibiotics in livestock farming, as it has been linked to higher risks from antibiotic-resistant bacteria.[50] An example of such bacteria strains is methicillin-resistant staphylococcus aureus, more commonly known as MRSA. This form of antibiotic-resistant bacteria is a leading cause of numerous severe or even fatal infections, which originated in European countries but has since made its way to North and South America. According to Gebreyes et al,[51] it has been more associated with hospital-developed illnesses in the past, but starting in the early 2000s, a new livestock-related strain of MRSA, Clonal Cluster 398, was discovered, having the potential to colonize humans. Amongst those who are the most vulnerable to MRSA are pig farm (swine) workers, whose risks are defined by the amount of time spent in the farm, the amount of inhaled contaminated dust, and density of pigs in the farm.[51] Furthermore, a Netherlands study, conducted by Voss et al., showed that swine workers were 760 times as likely to be infected by MRSA compared to the general population.[54] Apart from MRSA, MDR salmonella is amongst the many other infections related to traditional meat production, which particularly affects humans through the consumption of contaminated foods of animal origin, and has tens of millions of annual global cases.[51] By requiring large numbers of livestock for traditional meat production, and utilizing dangerously high amounts of antibiotics to prevent livestock from getting sick, not only are animals, their habitats, and the surrounding environment receiving the backlash, but also those who work in the animal food industry and live in local regions, by being at higher risks for a plethora of infectious diseases.

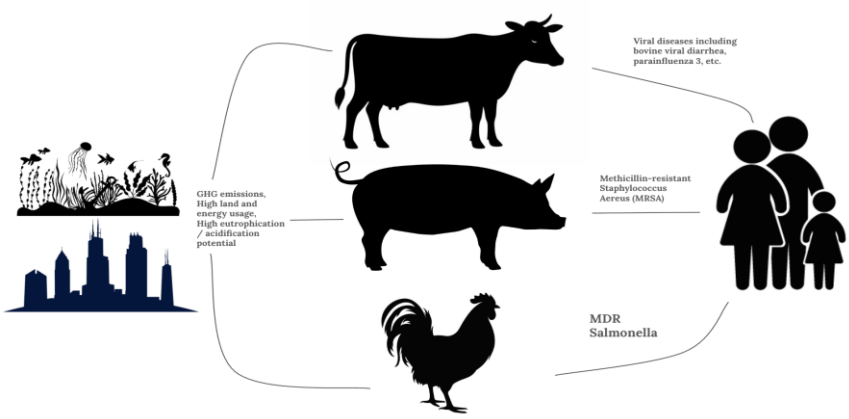

Figure 8: The Environmental and Public Health Impacts of Traditional Meat Production

General overview of the environmental and public health impacts derived from traditional meat production, grouped by cattle, pig, and chicken. Details sourced from Clark M and Tilman D[48], and Gebreyes et al.[51].

4.3 How Lab-Grown Meat can Protect Us and the Environment

To battle these negative environmental impacts and health risks, transitioning to lab-grown meats has the potential of decreasing greenhouse gas emissions by 78-96%, land usage by 99%, water usage by 82-96%, and energy requirements by 7-45%.[50] In order for cultivated meats to hold a smaller carbon footprint than conventional meats, companies in the industry should invest in renewable energy sources and prioritize energy efficiency, given that cultivated meat production could have a large demand for cumulative energy according to an ex-ante life cycle assessment by Sinke et al. [55, 56] Furthermore, by being developed and produced in a sterile medium without the usage of antibiotics, lab-grown meats would significantly lower the risks of antibiotic-resistant bacterial infections along with many other infectious diseases.[56] Human health would be preserved, the environment would benefit, and animals of different species and habitats would flourish. Lab-grown meats have great potential to foster safe and eco-friendly nutrition.

5. Conclusion

Cultured cell technology stands at the convergence of three critical global challenges: advanced medical treatment, sustainable food production, and environmental conservation. As this review demonstrates, the techniques pioneered in laboratory-grown meat production are not merely creating alternatives to conventional agriculture—they are fundamentally reshaping our approach to both nutrition and healing.

Perhaps most remarkably, the technologies developed for cultured meat are proving to be directly translatable to regenerative medicine. The scaffold engineering and stem cell cultivation techniques that create edible muscle and fat tissues are now being deployed in clinical trials for bladder reconstruction, vascular grafts, esophageal implants, and cartilage repair. Whether the goal is to produce marbled steak or repair damaged corneal epithelium, the fundamentals remain the same: creating living tissues outside the body that replicate native biological systems. The success of current clinical trials using cultured cell technologies validates this approach and suggests that the boundary between food science and regenerative medicine will continue to dissolve.

Recent advancements in transdifferentiation and co-cultivation highlight the nutritional potential of cultured meat beyond protein. Precise control of muscle and fat cell ratios and the ability to engineer phytonutrient content labels cultured meat as a potent, customizable superfood.

The transition to cultured meat production also marks a significant opportunity to reduce agriculture's ecological footprint. With potential reductions in emissions and resource usage, cultured meat offers a sustainable method to feed a growing global population. Its capacity to eliminate the public health risks associated with conventional animal agriculture–including antibiotic-resistant bacterial infections and zoonotic disease transmission–is equally important.

However, significant challenges remain before these technologies can achieve their full potential. In the clinical realm, long-term efficacy,

safety, and accessibility require ongoing investigation. Energy consumption in cultured meat production must also be carefully managed through renewable energy sources.

As we advance toward a future with cultured cell technology, continued investment in research and regulatory frameworks will be essential. The potential to transform food systems while revolutionizing medical treatment represents one of the most significant scientific opportunities of our time. The question is not whether cultured cells will heal and feed us, but how quickly we can overcome the remaining barriers to make this vision a reality for all.

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