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### **Experimental Study**

دراسة تعالج مشكلة



Production artificial meat in laboratory from animal cell culture and genetically engineered animal cell

أنتاج اللحوم صناعيا في المختبر من زراعة الخلايا الحيوانية والخلايا الحيوانية المهندسة

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#### **Abstract**

**Objectives:** The aim of the study: to know the pros and cons of cultivating animal cells in laboratories and cultivating genetically engineered animal cells and using them in industrial meat production in laboratories.

**Study design:** Meta-Analysis study design and Systematic Review study design.

**Backgrounds:** Cultivated meat, also known as cultured meat, is genuine animal meat (including seafood and organ meats) that is produced by cultivating animal cells directly. This production method eliminates the need to raise and farm animals for food. Cultivated meat is made of the same cell types that can be arranged in the same or similar structure as animal tissues, thus replicating the sensory and nutritional profiles of conventional meat. The benefits of cultivated meat, by nature of its more efficient production process, cultivated meat is expected to have a variety of benefits over conventional animal agriculture. Cell line engineering can take place in the form of adaptation or genetic engineering. Adaptation involves the serial subculture of a cell line in varying conditions along with selection over time.

**Methodology:** Growing, development and multiplication of animal cell tissue in laboratory, genetic engineering for animal cell tissue in laboratory and production artificial Meat in laboratory.

**Conclusions:** Cultivating animal cells in the laboratory is beneficial in terms of production, producing large quantities of meat produced in laboratories and in a very short time compared to growing whole animals in the field. One of the disadvantages of cultivating animal cells in the laboratory to produce meat industrially, through the continuous division of living cells in the laboratory, leads to unlimited mutations, e.g. uncontrolled, including random mutations and spontaneous mutations, as well as contamination with other microbes such as viruses and bacteria if there is not enough control. For continuous sterilization in the cultivation laboratory.

**Keywords:** Random recombination, Random mutation, Genetic variation and Spontaneous mutation.

### Introduction

Cultivated meat, also known as cultured meat, is genuine animal meat (including seafood and organ meats) that is produced by cultivating animal cells directly. This production method eliminates the need to raise and farm animals for food. Cultivated meat is made of the same cell types that can be arranged in the same or similar structure as animal tissues, thus replicating the sensory and nutritional profiles of conventional meat.

Decades of accumulated knowledge in cell culture, stem cell biology, tissue engineering, fermentation, and chemical and bioprocess engineering preceded the field of cultivated meat. Hundreds of companies and academic laboratories worldwide are conducting research across these disciplines to establish a new paradigm for manufacturing commodity meat products at industrial scales. Some companies are pursuing a similar strategy to create milk and other animal products.

The benefits of cultivated meat, by nature of its more efficient production process, cultivated meat is expected to have a variety of benefits over conventional animal agriculture. Prospective life cycle assessments indicate that cultivated meat will use significantly fewer resources and can reduce agriculture-related pollution and eutrophication. One study showed that cultivated meat, if produced using renewable energy, could reduce greenhouse gas emissions by up to 92% and land use by up to 90% compared to conventional beef. Additionally, commercial production is expected to occur entirely without antibiotics and is likely to result in fewer incidences of foodborne illnesses due to the lack of exposure risk from enteric pathogens.

Over the next few decades, cultivated meat and other alternative proteins are predicted to take significant market share from the \$1.7 trillion conventional meat and seafood industry. This shift will mitigate agriculture-related deforestation, biodiversity loss, antibiotic resistance, zoonotic disease outbreaks, and industrialized animal slaughter.

As of late 2022, several leading cultivated meat companies are transitioning to pilot-scale facilities that will manufacture the first wave of commercialized products following regulatory approval. The Singapore Food Agency approved the world's first cultivated chicken product for sale in December 2020, where it is currently sold in several restaurants, public food stalls, and a butchery. In November 2022, UPSIDE Foods completed the first United States Food and Drug Administration (FDA) pre-market consultation for its cultivated chicken produce.

Cell line engineering can take place in the form of adaptation or genetic engineering. Adaptation involves the serial subculture of a cell line in varying conditions along with selection over time. This process yields a cell line adapted to a new set of conditions or exhibiting a new trait. Common forms of adaptation include adaptation to serum-free medium, reduced requirements for growth factors, or suspension growth. Genetic engineering entails permanent changes by either removing, rearranging, or introducing DNA.

The current state of cell lines, many cell types can be used to cultivate meat According to an industry survey conducted in 2020, cultivated meat manufacturers are using a variety of starter cells, including skeletal muscle stem cells e.g. myosatellite cells, fibroblasts, mesenchymal stem cells, induced pluripotent and embryonic stem cells, and adipose-derived cells. Starter cells can also sometimes originate from specific organs to create other products. For example, cells from mammary glands can be used for milk production, and cells from livers for foie gras.

The most common method to acquire starter cells is by taking a cell sample from a live animal, which can be performed using minimally invasive methods. In some cases, these cells may also be acquired by biopsying a recently slaughtered animal where the tissue is still viable, which could be important for determining compliance to religious laws e.g. halal, kosher. In all cases, the acquired cells originate from healthy animals alongside extensive documentation that ensure the quality and traceability of the cells.

The majority of cultivated meat manufacturers work with well-characterized cell lines, which have the ability to continuously proliferate over time. Some producers

may use primary cells, which by definition have a finite life span. Currently, access to continuous cell lines from species used for cultivated meat production remains a major barrier for new research endeavors. The creation of new cell lines can be both time- and resource-intensive, often taking 6-18 months to derive and sufficiently characterize a single line. In medical research, the creation of large-scale cell line biorepositories is often nationally-sponsored, emphasizing their fundamental importance in advancing research. Similar government-backed projects for cultivated meat are underway in Singapore, but more are needed.

Cell line challenges, as described previously, there are many cell types that can be used as starting inputs for cultivated meat production. However, more research is needed to determine which cells will be best suited for large-scale manufacturing or the creation of specific product types. Intrinsic cell characteristics, such as suitability for suspension growth, doubling times, growth rates, metabolism, differentiation capacity, and genomic stability can vary between cell type and species.

These characteristics must be weighed alongside techno-economic models and bioprocess design considerations to inform cell line selection. However, this is challenging. Species used in cultivated meat production (especially aquatic animals) are much less researched than humans, mice, or hamsters, which have been the mainstay of the biomedical and biopharmaceutical industries.

Engineering cells can inform research and development, cell engineering can accelerate the development of cell lines suitable for cultivated meat. Engineering cell lines can dramatically improve the efficiency or productivity of the production process, or even influence end product attributes such as nutrition.

The current state of cell culture media, the cell culture media is the most important technology underlying the near-term success of the cultivated meat industry. Cell culture media is composed of two groups of components tailored to a specific cell or species

type.

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The first group of components, called the basal media, provides essential nutrients. It typically consists of a buffered solution containing glucose, inorganic salts, water-soluble vitamins, and amino acids. The second is a group of specific added factors that permit the long-term maintenance, proliferation, or differentiation of cells. These added factors are often recombinant proteins, growth factors or hormones, and other ingredients such as lipids and antioxidants.

Animal serum will not be used in large-scale production, while the basal media has persisted nearly unchanged since the 1950s, a transition away from other added factors originating from animal sources such as serum is still underway in many industries. The use of animal-derived components in cultivated meat production has prohibitive economic, and ethical constraints. Many companies have already publicly stated they are using medium formulations that are entirely animal-free, with some research groups and companies having published their protocols for serum-free proliferation and differentiation.

In Singapore, Eat Just's first cultivated chicken products were produced using small quantities of fetal bovine serum (FBS). However, the company received approval to sell cultivated chicken using serum-free media in early 2023. In the United States, UPSIDE Foods submitted information to the FDA showing their product can be created with or without FBS. In processes without FBS, purified bovine serum albumin was used. However, the company has stated that they intend to phase out the use of bovine serum albumin with recombinant forms of albumin protein.

The current state of bioprocess design, Bioreactors permit large-scale cell cultivation

The most important aspect of the bioprocess design is the bioreactor. Bioreactors (known colloquially as cultivators) provide the housing and control the conditions that enable cells to grow. For instance, bioreactors control the temperature, oxygen levels, and delivery of cell culture media.

They also enable monitoring of other important parameters such as metabolite levels, pH, and biomass accumulation. Different types of bioreactors have long-standing histories in other industries that rely on animal cell culture. Existing models are being

used by cultivated meat manufacturers this time. at Innovations in bioreactor technology represent a large whitespace opportunity, current models of bioreactors are not necessarily optimized for cultivated meat production. This is because the bioreactor and overall bioprocess design are influenced by the selection of cell type and its properties e.g., anchorage dependence, the cell culture media composition, and intended end product. Maintaining sterile cultures in a food grade facility will also be crucial to success The differentiation, maturation, and harvesting of cells for cultivated meat is likely to require unique innovations and bioreactor designs that address specific challenges for each of these phases.

### Methodology

### Study design

Meta-Analysis study design and Systematic review

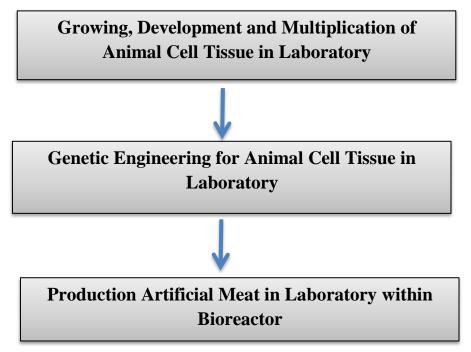


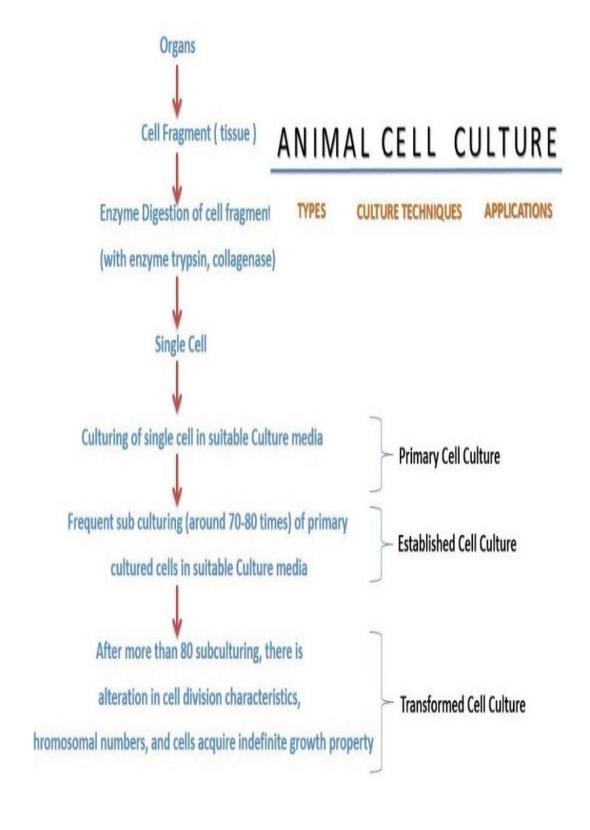
Figure (1): Scheme for this study.

# Steps production artificially Meat from animal cell tissue in laboratory

# Firstly: Growing, development and multiplication of animal cells in the laboratory.

- 1- Animal cells are grown artificially in a favorable environment in the form of animal cell culture.
- 2-The cells needed for animal culture should come from multicellular eukaryotes and their established cell lines.
- 3-The technique of animal cell culture is used to separate and cultivate cells from animals under artificial conditions.
- 4-A cell line can be maintained as a distinct entity from its original source using this technique, which was developed for specific laboratory studies.
- 5-To develop animal cell culture techniques, basic tissue culture media were developed in order to enable the work of so many different types of cells under different conditions.
- 6-Cells isolated from various animals have been cultured in vitro to help discover different functions and mechanisms of behavior.
- 7-Cancer research, vaccine production, and gene therapy are some of the areas where animal cell cultures find the most application.
- 8-Cells grown on artificial media require more nutrients and growth factors than microorganisms, since they grow more slowly.
- 9-The artificial media now offer both the possibility of culturing differentiated cells and those that are undifferentiated.
- 10-In vitro animal cell cultures can be initiated using different types of cells, and in vitro organ cultures can be initiated using complex structures like organs.

11-The culture process can use any type of tissue, cell, or organ depending on the purpose and application.

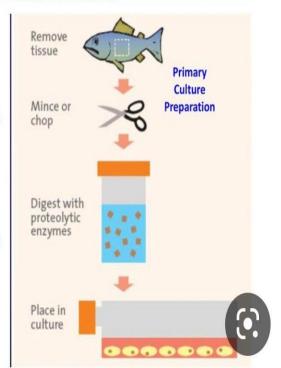


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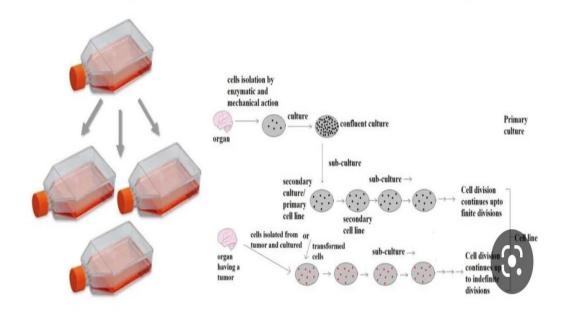
# **Types of Cell culture**

### 1. Primary Cultures

- Derived directly from excised tissue and cultured either as:
- Outgrowth of excised tissue in culture
- Dissociation into single cells (by enzymatic digestion or mechanical dispersion).



# **Animal Cell Culture**



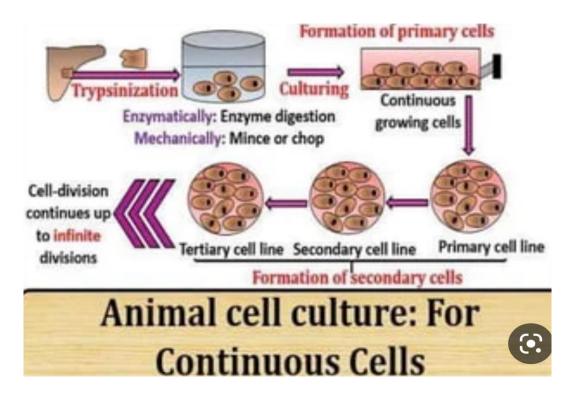


Figure (2): Growing, development and multiplication of animal cells in the laboratory.

# Secondly: Genetic engineering (genetic manipulation) of animal cells in the laboratory

- 1-PCR
- 2-Restriction enzyme
- 3-Genetic Engineering (Cloning)
- 4-Recombination (Transformation)
- 5-Screening of successful offspring cloned cells in the process of genetic transformation (genetically engineered) and novel clone [1 and 2].

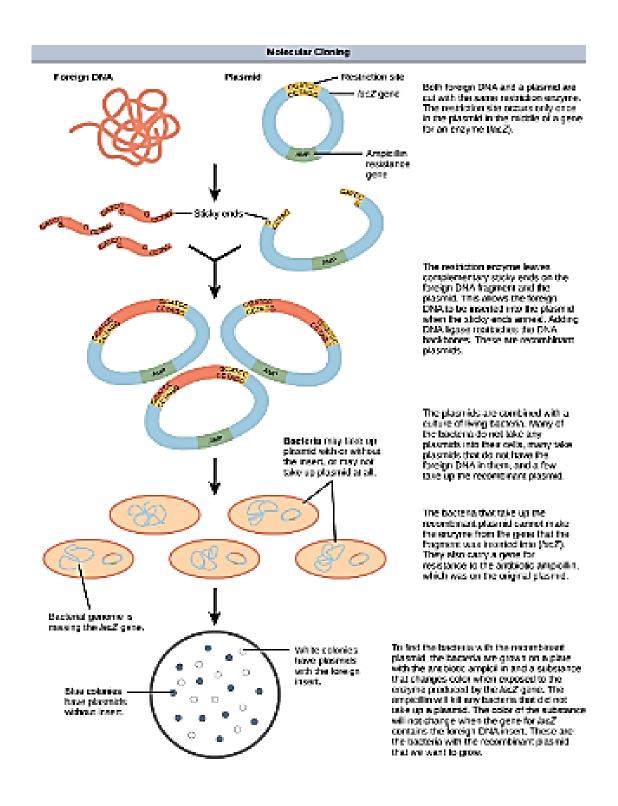


Figure (3): Genetic engineering (genetic manipulation) of animal cells in the laboratory.

## Third: Producing Meat industrially in the laboratory through culturing animal tissue in the laboratory

- 1-The manufacturing process begins with acquiring and banking stem cells from an animal.
- 2-These cells are then grown in bioreactors (known colloquially as cultivators) at high densities and volumes.

Similar to what happens inside an animal's body, the cells are fed an oxygen-rich cell culture medium made up of basic nutrients such as amino acids, glucose, vitamins, and inorganic salts, and supplemented with growth factors and other proteins.

- 3-Changes in the medium composition, often in tandem with cues from a scaffolding structure, trigger immature cells to differentiate into the skeletal muscle, fat and connective tissues that make up meat.
- 4-The differentiated cells are then harvested, prepared, and packaged into final products.
- 5-This process is expected to take between 2-8 weeks, depending on what kind of meat is being cultivated [3].

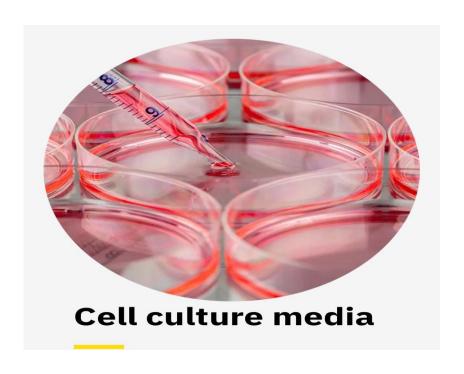




Figure (4): Producing meat industrially in the laboratory through culturing animal cells in the laboratory

### **Conclusions**

1-Cultivating animal cells in the laboratory is beneficial in terms of production, producing large quantities of meat produced in laboratories and in a very short time compared to growing whole animals in the field.

2-One of the disadvantages of cultivating animal cells in the laboratory to produce meat industrially, through the continuous division of living cells in the laboratory, leads to unlimited mutations, e.g. uncontrolled, including random mutations and spontaneous mutations, as well as contamination with other microbes such as viruses and bacteria if there is not enough control. For continuous sterilization in the cultivation laboratory.

3-One of the benefits of genetic engineering of animal cells is the production of living organisms and new cells that carry new desirable characteristics and are important in production. Among them, production can be increased exponentially from the previous one through the introduction of genes from genetically different organisms and the production of new genetic heterogeneity that is beneficial to humans.

4-One of the harms of genetic engineering of animal cells is that random recombination of genes within animal cells can occur, which leads to useless mutations that can lead to many diseases, including tumors such as cancer.

#### **Recommendations**

1-Using the cultivation of young animal cells with a short life is better than cultivating animal cells with a long life in order to get rid of random mutations and spontaneous mutations.

2-Using a bioreactor to develop and multiply animal cells under well-controlled conditions so that they are free from contamination by microbes such as bacteria and viruses.

3-If genetically engineered animal cells are used, they can be used while they possess genes that are resistant to infection with microbes and viruses, in addition to the new genes encoding the new trait desired in production.

### **About author**

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Professor Emeritus of World Sciences

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Author of books and translator books

Inventor of more than 13 patents accepted in Iraq and published in America

strains are registered in the American Genome Bank NCBI 7

Iraqi bacterial strains named after Nebras Rada Mohammed

holds gold medals and decorations for more than 150 medals and gold medals

She holds books of thanks and appreciation for more than 100 books of thanks and appreciation and certificates of appreciation

Member of more than 60 international and local associations

Recipient of many awards in different countries around the world, including

Best Community Personality Award 2020

Best Arab Woman Award in the Middle East 2020

WIPO World Intellectual Property Award

Best Research Award in the Middle East 2020

Best Research Award 2019 in Egypt / Sharm El-Sheikh

awards from Toronto, Canada &

First place award for invention from America for the patent of clot treatment

First place award from America for the patent of propolis purification

First place award from America for patent colistin gene

Honoring the best Arab scientist from the Atwar Academy for Scientific and Research Development

Wissam Mashoua is a scientist from Malaysia and Britain / London

Best distinguished inventor from America

Scientific creativity

Scientific excellence

The best Arab scientist

PhD in free media

A doctorate in postgraduate studiesa professional doctorate

An honorary doctorate

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The account of the researcher, Dr. Nebras Rada Mohammed

1-Researchgate account

https://www.researchgate.net/profile/Nebras-Mohammed-2

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