CELLULAR AGRICULTURE

THE FUTURE OF FOOD

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We live on a planet that is starkly different from that it was in the past, transformed completely by the number and activities of just one species- the human species! The progress has hugely impacted earth's environment and our climate. While technology is hailed and nailed to be the cause of the climate change crisis, it ironically, is the one which will be bail us out, just as did for the ozone hole!

The data brings out the fact that 26% of Earth's ice-free surface is used for livestock farming, nearly 70% of all agricultural land. In addition, 27-29% of freshwater footprint is used for the production of animal products. Livestock farming is a top contributor to deforestation, land degradation, water pollution and desertification. Considering the fact that anticipated global demand for animal products to increase by 70% in 2050, it becomes extremely important to explore different ways to feed the growing population without destructing the earth's resources.

Here we share interesting technologies in the area of Food which holds promise to confront climate change challenges- Cellular Agriculture being the one. Cellular agriculture and 3D food printing, the two new technologies that are expected to change the way people will source food from in near future. These technologies lead to animal-free, cultured & plant based versions of meat, milk, eggs and leather or in other words, they are milk without cow, eggs without hen and meat without animal. Over the last three years, several cellular agricultural startups have been created applying cellular agriculture to make a number of agricultural products and consumables.

In fact, "Vegetarian Meat" based on plant sources is now available in India too. These alternate forms of growing meat have lead to saving many resources detrimental to environment as well as created better acceptance by vegetarian segment of society from nutrition point of view and also reduction in cruelty towards animals.It offers significant promise for a more safe and diverse food system in a sustainable manner. If monitored and managed appropriately, cellular agriculture could allow humans to produce more food on less land than ever before while simultaneously addressing environmental problems.

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Cellular Agriculture – The Future of Food

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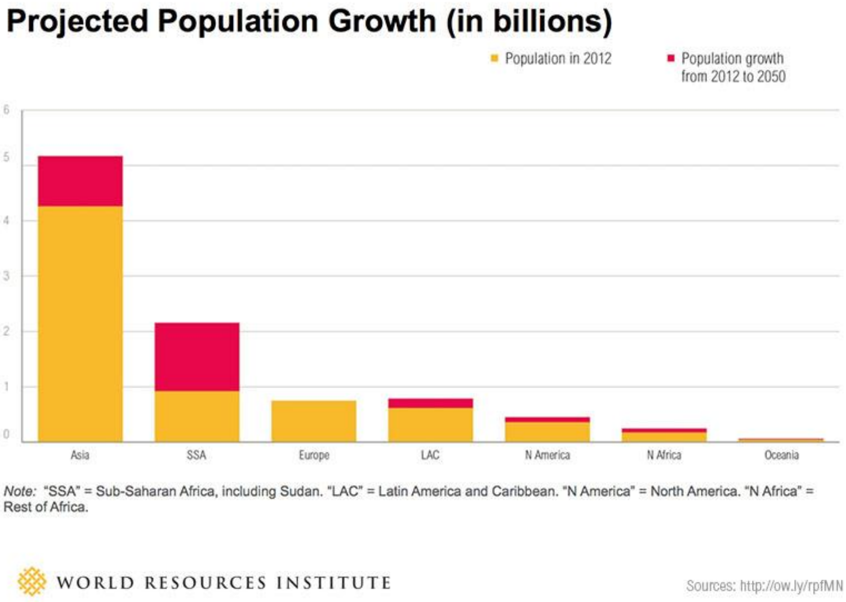
https://edition.cnn.com/2018/03/01/health/clean-in-vitro-meat-food/index.html

1.1 UNDERSTANDING THE NEED

(a) Demand for animal food

The world population is growing at an alarming rate.



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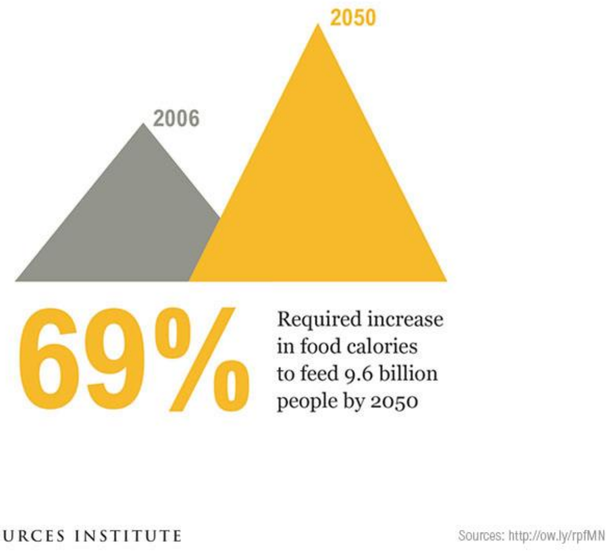


Source: http://www.wri.org/sites/default/files/uploads/population_growth_0.jpg

To feed millions of people and meet their dietary preferences, the livestock sector has been expanding incessantly. Estimates indicate that for the last six decades the global meat production has risen three times and expected to reach 300 million ton by the year 2020 (Alexandratos and Bruinsma 2012). Part of the dietary preference is also due to rising affluence and urbanization (Tuomisto and Teixeira de Mattos 2011). Thus, the exponential growth of livestock meat sector poses enormous challenges to sustainable food production.

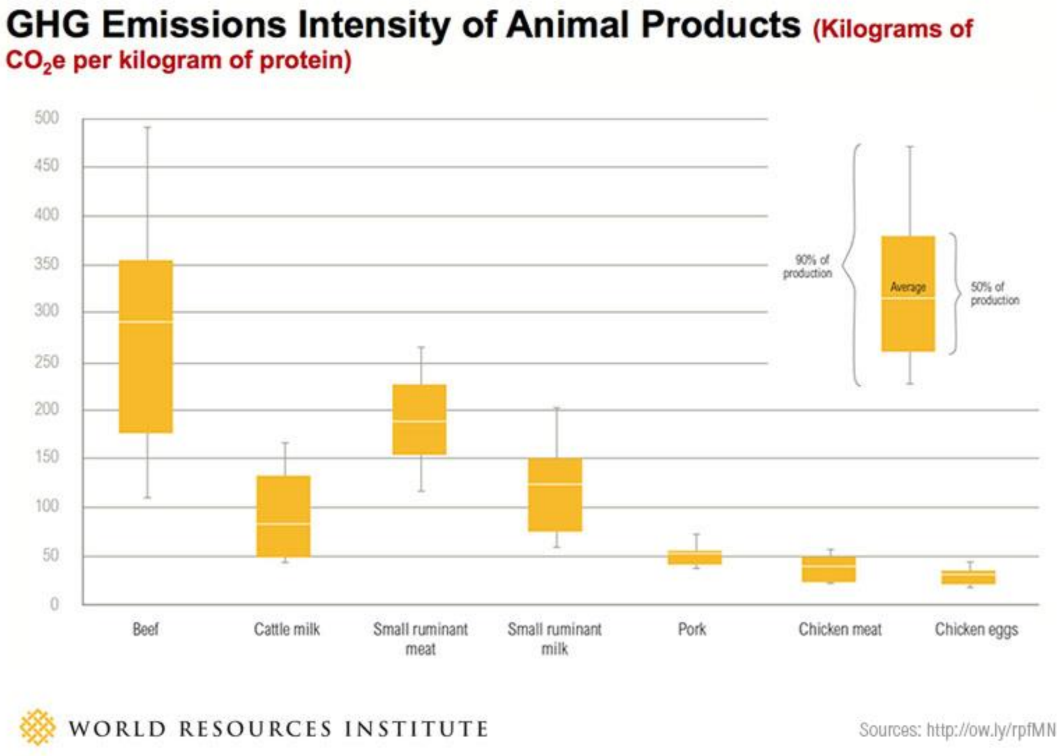
Overall, it seems the global demand for food production may increase by 70% (latest UN estimates) due to population growth. To sustain the livestock production, approx. 670 million tons of cereals are used as livestock feed annually, which is equivalent to over one-third of cereals consumed globally (Speedy 2003). This further constrains limited resources available to feed the enormous and rapidly growing population of the world.

To meet the global demand for food, the idea of replacing the livestock meat with the lab-grown meat (also called in vitro meat, synthetic meat or artificial meat) was proposed more than a decade back (Edelman, 2003). The idea was to eliminate animal slaughter and feed the population with ethically produced meat.

In addition to satisfying the hunger of a large population, there are many other pressing reasons for this paradigm shift. The key issue is to find lasting solutions to the environmental damage caused by the massive production of livestock animals.

(b) Global warming

Convincing scientific evidence points to the emission of methane (CH_4) and nitrous oxide (N_2O), by livestock animals. It has been found that both methane and nitrous oxide are much more harming greenhouse gases than carbon dioxide (Lesschen et al. 2011; UNEP GEAS 2012). Navigating the numbers, it seems about 9 % of emissions from agricultural sector consist of Carbon dioxide, 35–45 % of methane and 45–55 % of nitrous oxide (McMichael et al, 2007).



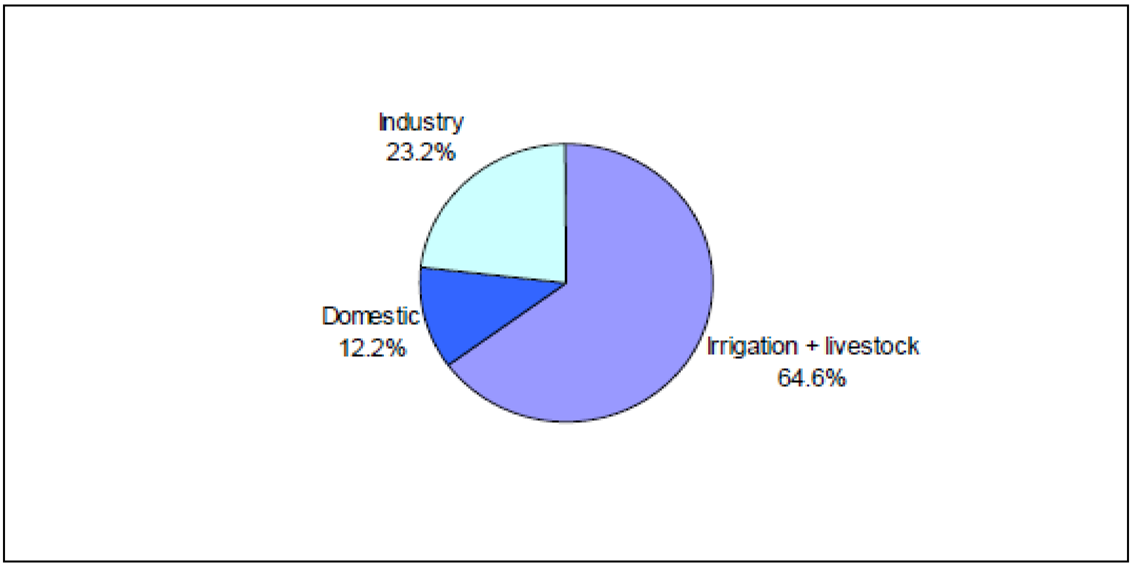
http://www.wri.org/sites/default/files/uploads/emissions_from_animal_products_0.jpg

The magnitude of these emissions is continuously evaluated and discussed. However, it is clear that livestock is a major anthropogenic source of atmospheric pollutants, such as ammonia, nitrous oxide, methane and carbon dioxide (Gold 2004). Estimates indicate that about 70–80 % of dietary nitrogen fed to cattle, pigs and laying hens is excreted contributing significantly to global warming (UNEP GEAS 2012). This is a clear indication of the magnitude of environmental damage caused by these gases. Besides, these crops required to grow animal feed and fertilizers produced to sustain the productivity of the crops add to the severity (Tuomisto and Mattos, 2011). The manure of industrially farmed animals generates ammonia, methane, hydrogen sulphide, carbon monoxide, cyanide, phosphorus, nitrates and heavy metals along with over 100 microbial pathogens like salmonella, cryptosporidium, streptococci, and Giardia (Goffman, 2012). To sustain the production of animals, crops need to be grown and sustained by using fertilizers, pesticides, herbicides, insecticides, and fungicides. The immensely elevated nitrate levels cause significant direct and indirect harm to the environment.

(c) Depletion of fresh water and land

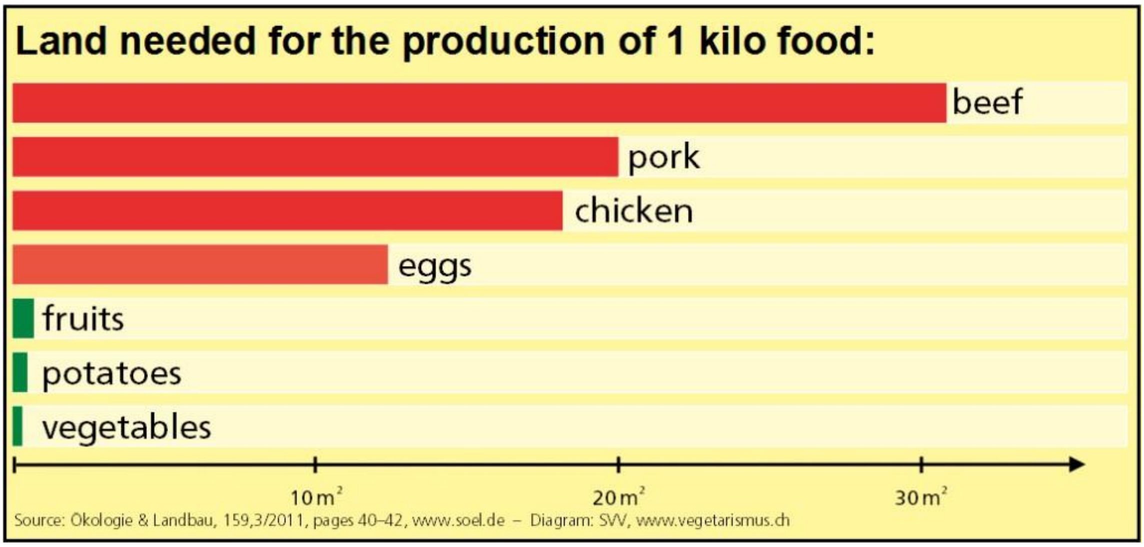
The livestock sector uses huge quantities of water for producing feeds, rearing, and sanitation of animals. Estimates indicate that the livestock sector consumes over 8 % of global human water usage (Goffman, 2012), e.g., in Brazil, the beef production requires 15,500 m3/t of water and chicken 3918 m3/t (Gold, 2004). These numbers of massively converting fresh water into wastewater are alarming and pose a significant risk to human survival.

FIGURE 1
Water withdrawal by sector
Total 554.1 km^3 in 2005



http://www.fao.org/nr/water/aquastat/countries_regions/CHN/

It has been noticed that farmed animals produce enormous waste that far exceeds that of the human population. It seems that in the United States alone, the cattle produce 130 times more waste than humans. Estimates indicate that water recycled from livestock manure may be responsible for 33% of global nitrogen and phosphorous pollution, 50% of antibiotic pollution, and 37% of toxic heavy metals found in freshwater. Approx 37% of pesticides have been found to end up in the water supply from livestock production (Edwards, 2017)



http://www.vegetarismus.ch/info/eoeko.htm

It may be relevant to note that fresh water is not always available to process or clean the meat. Many slaughterhouses reuse water mixed with blood and waste leading to significant health risks. Added to this is the massive slaughtering of cattle on festivals that leads to rivers of blood in some countries. The blood seeps into drains polluting both standing and moving water bodies

Reports indicate that livestock farming takes up to 30% of earth's land surface. Of that, 70% of arable land is consumed in livestock farming (Edwards, 2017). Some of the reports are truly alarming that indicate approx 70% of deforested areas in the Amazon rainforest are used as pastures, and a significant fraction of the remaining 30% is used to raise animal feed crops.

(d) Impact on human health

Reports indicate that 60% of human diseases and 75% of the emerging human diseases have origins in animal transmission (Edwards, 2017) For example, bovine spongiform encephalopathy (BSE), Swine and avian influenza have been found to be transmitted from animals (Vleeschauwer et al, 2009) The intensification of livestock farming, (Edwards, 2017) will only worsen the fragile situation.

Antibiotics are widely used to accelerate animal tissue growth, and keep them in good health till slaughter. The uncontrolled practice of using antibiotics for livestock animals has led to accumulation in the waterways (Bonne, 2004) and humans and is responsible for the significant rise in drug-resistant pathogen strains (Timothy et al,

2012) The World Health Organization considers this one of the biggest threats to global health. (WHO, 2018).

(e) Animal well being

Animals are living beings full of emotions. They feel pleasure and pain just like humans. Any suffering inflicted upon them by humans for the sole purpose of raising animals for food is insensitive, unethical and vicious. Massive animal farming often comes with disregard for their hygiene, safety, good health, and welfare. Animal farming consumes enormous land and water resources. Their high market demand often results in their torture both in the form of hormonal injections for biomass increase and saving money on their welfare, with the result that animal welfare is considered lowest priority and measures are reduced to a bare minimum. On paper, there may be nice documentation of animal welfare protocols. However, in reality, animal welfare is significantly ignored in factory farms. Animals are brutally treated before killing them for food.

https://www.mirror.co.uk/news/uk-news/secret-film-exposes-chicken-factory-1338652

As an example, “broiler chicken”, optimized for obesity and rapid maturation is often reared in cramped conditions leading to immense suffering, fractured bones, and infections and so on. Worse at the time to transport to slaughterhouses, they are hung upside down in groups generating immense pain and wound. Furthermore, broilers are pushed into cramped transport containers and treated in inhumane conditions till their end of life. Despite standard guidelines to ensure animal welfare, the implementation is still weak and poorly. Animals are subjected to brutal amputations while alive. It is common for large meat producers to refuse public inspection of their farms and slaughterhouses.

The world needs a credible alternative for meat supply ethically and safely.

1.2 CELLULAR AGRICULTURE – A BRIEF INTRODUCTION

Cellular Agriculture is a multi-disciplinary branch of science encompassing biotechnology, medicine, and farming. It is a nascent technology that allows meat and other agricultural products to be cultured from cells in a fermentor or a bioreactor rather than harvested from livestock on a farm. It designs new mechanisms to produce existing agriculture products especially animal products from cell cultures rather than the bodies of living organisms. In other words, Cellular Agriculture is the technology with the use of which the real dairy products are produced without exploiting cows, eggs without hens and meat without having living animals slaughtered.

While the main use of this technology has been for food applications, particularly in vitro or cultured meat, called ‘clean meat', cellular agriculture can be used to create any kind of agricultural product, including those that never involved animals, to begin with, eggs, leather, milk, fragrances, gelatin and silk.

Numerous animal-free protein products are hitting the shelves today, and with them are a variety of production methods. Cellular agriculture should not be mingled with another cutting-edge technology to produce plant-based meats. Plant-based meats aim to replicate the taste and texture of conventional meat. Cellular agriculture differs from the plant-based products like Beyond Meat's burgers, Hampton Creek's line of condiments and baking products and the varieties of nut-based milk in the market. Instead of making plant-based substitutes that try to impersonate the taste and texture of meat and dairy, cellular agriculture uses methods of tissue engineering to food production to create meat and dairy products that are molecularly similar to those made via conventional means. This can revolutionize the supply chain of animal products to continue to provide affordable and sustainable food and other materials to a growing population.

Cellular agriculture allows us to make milk, eggs, meat, leather, fur, perfumes and other animal products but this dossier will majorly be focussing on clean meat. In recent years some cellular agriculture companies and non-profit organizations promoting the technology have emerged due to technological advances and increasing apprehension over the animal welfare and rights, environmental and public health problems linked with conventional animal agriculture.

1.3 TECHNOLOGY INVOLVED

(a) Historical

The origin of cell culture may be traced back to the late 19^{th} century when Claude Bernard (1878) proposed that physiological systems of an organism can be maintained even after the death of the organism. This was quickly followed by the proof of the concept when Roux (1885) demonstrated maintenance of embryonic chick cells in saline culture. Nearly a decade later, Loeb (1897) reported survival of blood cells outside the body. In 1907 Harrison demonstrated the maintenance of frog nerve cells in vitro. Five years later, Carrel established aseptic techniques for cell culture. By mid-1920s people were sensitized towards artificially maintaining the cells outside the body leading to the formation of ECACC for cell culture preservation. Between 1920 to 1930, differentiation of cells in vitro and fibroblast cell culture was reported.

This gave impetus to the development of ATCC for developing standard techniques and preservation of cells. The culture of cells, preparation of antibodies and vaccine was actively followed between 1940 and 1950. Soon after, the first mouse fibroblast cell line and human cell line was developed.

By mid-1950s a well-defined media for cell culture was established (Eagle, 1955), the lifespan of human cells growing in vitro was defined (Hayflick, 1965) leading to the development of first hybridoma cell line (Kohler and Milstein, 1975).

Privatization of biotechnology took off in a major way leading to the production of first therapeutic protein in cell culture by Genentech in 1983. The developments in cell culture technology in the next three decades were rapid, widespread and made significant inroads in the public and private institutions. Concepts and methods of tissue engineering surfaced (Atala & Lanza, 2002) leading to the development of induced pluripotent cells (Yamanaka, 2006) and development of 3D bioprinting techniques (Atala et al, 2010).

(b) Cell culture fundamentals

For successful cell culture, one needs sterile work area ensured by pressurized air that passes through HEPA (High-Efficiency Particle Air Filter) filters, incubators, pure and sterile water, cold storage, microscopes and culture ware, the most common being specially treated polystyrene.

The culture medium is prepared to provide food for the cells and maintain an optimal pH. In general, media is a combination of amino acids, fatty acids, sugars, ions, vitamins, cofactors inorganic salts and so on. Natural media that are used to grow cells in vitro may have plasma/serum or tissue extracts. In contrast, synthetic media is prepared artificially by adding nutrients, vitamins carbohydrates, salts etc., e.g., minimal essential medium, RPMI 1640 medium and so on.

Cultures are mostly maintained at pH 7 – 7.4. Due to metabolic activities, the pH gets lowered over time and may result in cell growth inhibition. To slow down pH change bicarbonate based buffers are used in addition to maintaining the culture in 5% CO2 that serves as a gaseous buffer. Furthermore, a change in osmolality (i.e., number of dissolved particles in a fluid) can affect cell growth. Culture media are formulated in such a way that the osmolality is maintained around 300 mOsm.

Growth requirements of cells demand supply of amino acids not synthesized by the cells. For example, glutamine is required by most cells in addition to essential amino acids like cysteine and tyrosine. To ensure that cell culture is clear of any infection, antibiotics (and in some instances) antifungal substances are added to the cell culture medium.

Cell culture may be primary (i.e., the tissue is surgically removed and cultured in vitro) or derived from cell lines. Primary cell culture involves growing cells directly from the tissue. The other method is digesting the tissue by enzymes and creating a suspension of cells for culture. Primary cells have advantages of resembling closest to the source wherefrom cells were derived. However, loss of cells during enzymatic digestion, damage to the cell membrane and loss of viable cells, is a typical trade-off.

The subculture of cells comes into picture when cells have grown to confluency and need to be transferred to another vessel for culture. Cells come with three basic morphologies: epithelial (cells adhere to the substrates and appear flattened / polygonal), lymphoblast like and fibroblast types. The culture of cells is highly technical and requires significant experience to maintain a right growth trajectory and aseptic conditions. Most of the cells have a finite lifespan. However, when cell get transformed into cell lines, they become immortal.

In general, cell cultures provide a good model for studying the effect of drugs, the aging process, toxicity testing, and disease research and so on. Furthermore, they can also be used as factories to produce various chemicals, and proteins.

(e) Self-organizing method

With an aim to create highly structured meat, innovative approaches to self-organized techniques are required (Dennis and Kosnik, 2000). Back in 1912, researchers Alexis Carrel demonstrated the feasibility of keeping chick heart muscle alive in a petri dish using suitable culture medium and conditions. Further advances along the lines of self-organizing tissue grown in vitro, had to wait till 2002 when tissue engineering techniques were matured. In a landmark paper (Bejaminson et al, 2002), the skeletal muscle explants from goldfish were reported to be grown artificially for a week, and interesting patterns of cell growth beyond the original explant were observed covering close to 80% of the surface area of the culture vessel. Authors of this work used a combination of fetal bovine serum, fishmeal extract, shiitake extract and maitake extract. Furthermore, the possibility of maintaining chicken muscle cells for a prolonged period of 8 weeks was also demonstrated (Wolfson, 2002).

Though proof of the concept was made available, the bottleneck was an inability to develop a blood circulatory system within cells radiating out of the explants. Fast forwarding to 2018 and this still an unsolved problem. Sometime in future, if people can create a 3D mass of muscles with bones, cartilages and blood vessels self-organizing themselves at their natural positions, the science of in vitro meat will truly be path-breaking. (e) Scaffold-based technique: In the scaffold based technique, embryonic myoblasts or adult skeletal muscle cells are attached to a scaffold and then grown in a culture medium (Kosnik et al, 2003). Cells may be grown on collagen beads swimming in culture media or cells may be attached to a collagen meshwork and programmed to produce along with a specific track. Alternatively, in place of collagen other edible proteins may be used. In both the situations, the outcome is a three-dimensional structure of meat. Cells may be further proliferated, differentiated and fused. Also, stem cells may be used to differentiate into various cell types and give a look of a natural meat. (Williams, 2012). An ideal key property of a scaffold would be mechanical stretching and contraction that would program the cell growth along a predefined track. In the past, cytodex-3 microcarrier beads have been used as scaffolds in rotary bioreactors. However, in such beads, the flexibility and stretchability are missing. In future, one could try various edible and stretchable polymers such as collagen, cellulose and so on.

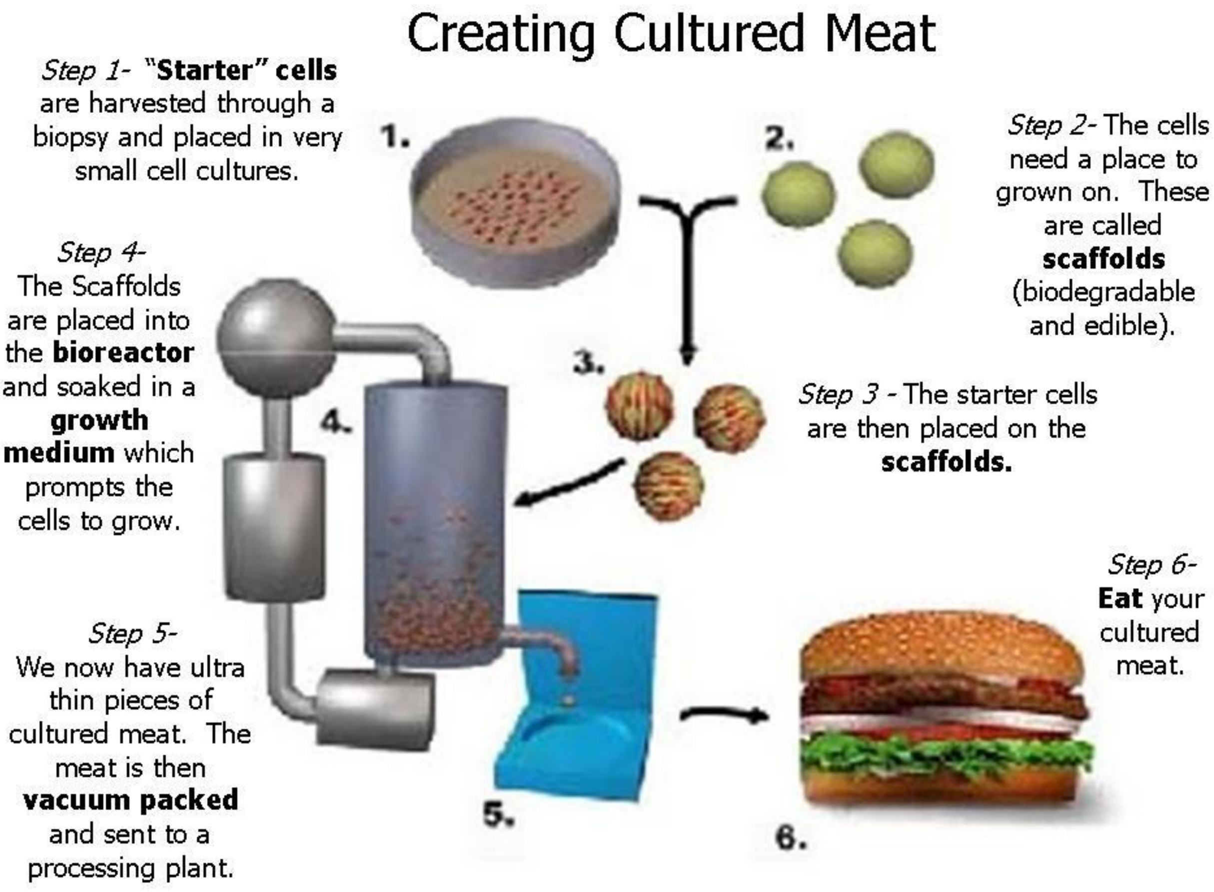
(c) Clean meat

The idea to create artificial meat may be traced to 1930s when Frederick E Smith wrote: “It will not be required to go through the time-consuming process of rearing a bullock to eat its steak. From one ‘parent' steak of choice tenderness, it will be possible to grow as large and as juicy a steak as can be desired” (Birkenhead and Smith, 1930). Winston Churchill followed it up with his quote “Fifty years hence we shall escape the absurdity of growing a whole chicken to eat the breast or wing by growing these parts separately under a suitable medium (Churchill, 1932).

https://www.fdli.org/2018/02/update-laws-regulations-concerning-cell-cultured-meat-cellular-agriculture/

The technology used in the cellular agriculture is a blend of different disciplines viz tissue engineering, synthetic biology and material sciences. The various research tools involved in cellular agriculture are cell lines, growth media, scaffold materials, 3D tissue systems and scaling technologies. Cells from a particular species and tissue type are assembled on a scaffold which aids the growth of cells with serum (food for the cells to feed on while they grow) in an environment that promotes growth. No living being is required for the production of either foodstuffs or materials. Significant six steps involved in the cellular agriculture may be seen in the diagram below.

(d) Steps involved



Source: https://the-fringe.com/thread-in_vitro_meat (Cultured meat; manufacturing of meat products through "tissue-engineering" technology. By Stark Industries, 05-31-2017)

The ideal criteria for the cells to be used for cultured meat production include proliferative nature, immortality, and ability to grow independent of any surface and serum and tissue forming ability. These may be embryonic stem cells, adult stem cells or myoblasts. Stem cells proliferate at a high rate, but it is challenging to direct them to grow in a particular way. Fully developed muscle cells have complete development as a muscle but proliferate hardly at all. Therefore, cells like myoblasts are ideal which have already differentiated to an extent and also have the ability to divide. The growth media uses a fetal bovine serum (FBS) for supplying cells with nutrients and stimulating growth factors. Bioreactors of increasing volume need to be created to make the whole process economically viable. To culture three-

dimensional meats, the cells are grown on a scaffold which ideally should be edible so that it is not required to be separated at the end of the process.

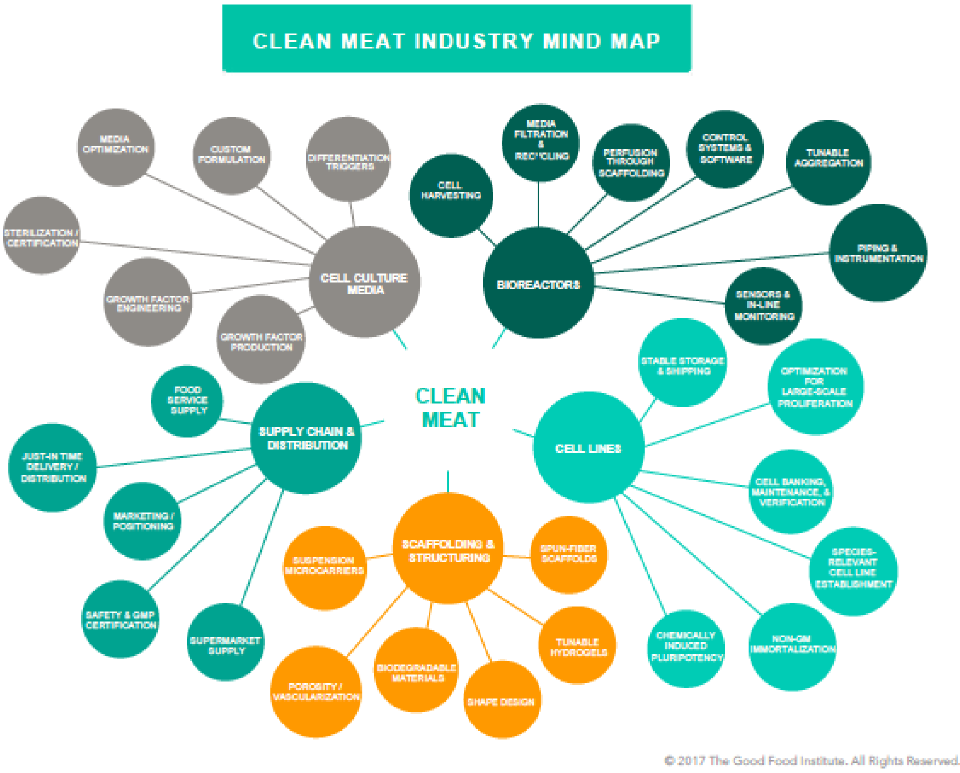
The process of developing cultured meat requires muscle cells and then applying a protein that kick-starts tissue growth. Genetic engineering is not required, although a method to extract muscle tissue from other tissues is needed. Once this is achieved, the extracted cells can be replicated to produce trillions of copies. As the process starts, meat is produced. In theory, it is anticipated calculation that two months of cultured meat production can end up in about 50,000 tons of meat from just ten pork muscle cells. Cultured meat is often produced as strips of muscle fibre. The culturing process occurs under desirable conditions inside a bioreactor explicitly designed for the purpose. Preservatives are added to prevent microbial growth. An alternative approach is to use the artificial circulatory system to distribute nutrients and oxygen, with the idea of producing cultured meat on a larger scale.

Tissue engineering is a process wherein the tissues are made outside the body and is a relatively new scientific approach, with a focus on clinical applications such as growing skin for burn patients or organs for patients requiring organ transplantation. In our bodies, blood vessels carry nutrients and remove waste products from our tissues. This allows the tissues in our bodies to be quite thick, but if the vessels are absent, the cells do not have access to nutrients what they need to grow. In culture, tissues can only grow about 0.5mm thick without vessels. For growing organs for medical purposes, this is a problem. But for growing cultured meat, it is not.

Cultured meat name is misleading in the sense that it gives a picture that the meat is produced in Petri plates and laboratories, but this is not true. The labs and petri plates may be involved in the initial stages, but scaled production will happen in large meat bioreactors or fermentors. It is unjustified to call it as lab-grown meat as well because there will be no labs involved in the commercial production.

The name clean meat is the most accurate name not only because it is obtained without animal slaying but also because of the environmental benefits and decrease in foodborne pathogens and drug residues. This is the term which industry has converged on and is likely to be used in India as well.

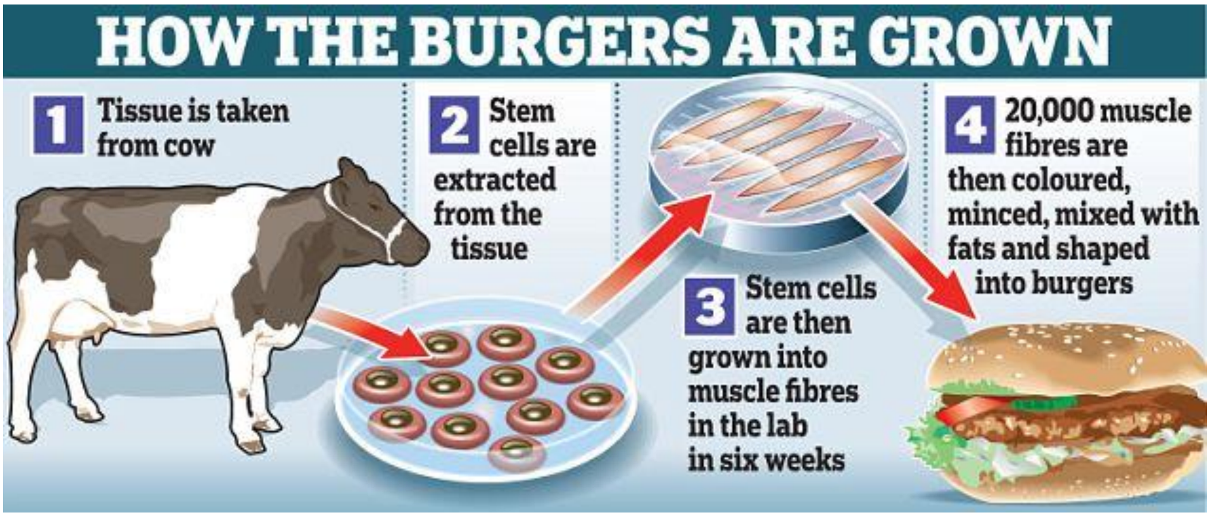
There are therefore four main technology elements, which require specialized research and development: cell lines, cell culture media, scaffolds, and bioreactors. Each of these technology elements represents a significant area of opportunity for private industry and can draw on decades of advancement and investment in R&D.



(f) Stem cells

Stem cells are undifferentiated cells in organisms that divide to produce more stem cells. Two types of stem cells exist in multicellular organisms: embryonic stem cells that are found early in development and adult stem cells that are found in some regions of adult organisms like bone marrow, adipose tissue, and umbilical cord blood. A stem cell has the ability of self-renewal and also differentiate into specialized cells types, e.g., hematopoietic system

The science of stem cell culture and programmed differentiation has significantly advanced. Researchers have used background experimental data and hands-on experience in stem cell differentiation to grow myoblasts (muscle cells) with intent to produce meatballs. Furthermore, satellite cells are used to form myotubes and myofibrils (Collins et al. 2005).



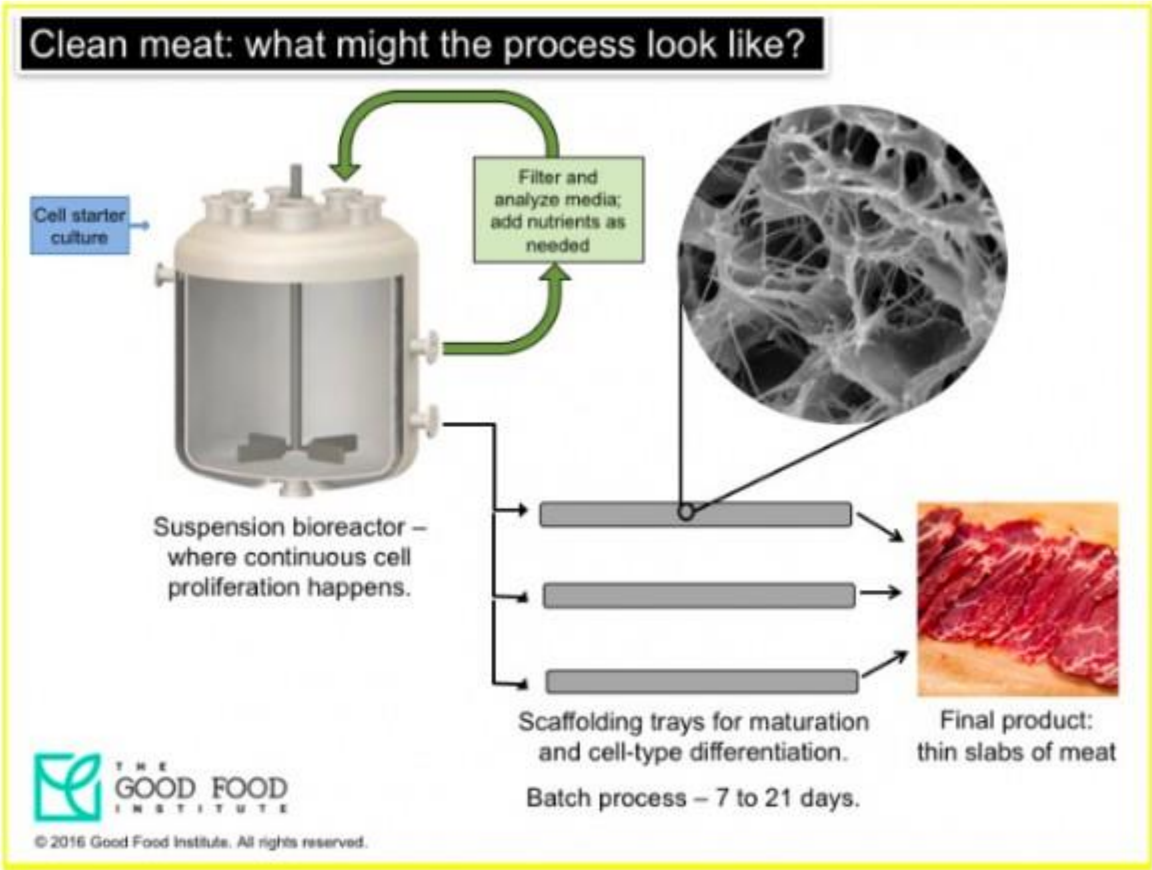
http://www.dailymail.co.uk/sciencetech/article-3275913/Lab-grown-burgers-menu-2020-Scientists-set-company-make-stem-cell-meat-affordable-reality.html

Adult stem cells are preferred sources for cultured meat generation due to ethical issues. Adult stem cells obtained from pigs (Zeng et al 2006) and cattle (Kook et al2006) have been proliferated successfully in vitro. Besides, adipose tissue-derived adult stem cells have also been used for cultured meat production (Burkholder, 2007), as they immortalize at high efficiency (Rubio et al2005). Mature adipocytes have been found to dedifferentiate into multipotent cells with an innate property towards transdifferentiation into skeletal myocytes (Kazama et al. 2008).

Myosatelite cells are considered most suitable for culturing meat (Edelman et al. 2005) either alone or in combination with fat cells (Edelman et al. 2005).

(g) Culturing meat in bioreactors

For the large-scale commercial production of cultured meat, a bioreactor based growth of cells is clearly a way forward. The key advantages of a bioreactor are a near-continuous suspension of cells, low fluid shear, and high output. The culture medium supplemented with serum and growth factors forms the foundation of cellular growth. Additives like esphingosine 1-phosphate and amino-acid rich mushroom extracts have been suggested for the serum-based media (Datar and Betti 2010).



http://www.gfi.org/clean-meats-path-to-commercialization

Growth factors produced by the muscle cells themselves and other cell types help in further proliferation of the mass of the cells (Edelman et al. 2005). As the cell proliferation enters differentiation and maturation phase, one may require a change in the culture media, as by-products and pH changes can slow down / inhibit the growth.

Bioreactors are used for growing cells large scale under controlled conditions of temperatures, pH, oxygen levels, nutrients and so on. Historically, bioreactors have been used to make pharmaceuticals, vaccines, or antibodies. With the evolution of needs, bioreactor technologies have evolved too. Recently, rotating bioreactors were used for the production of skeletal muscle tissue (Van der Weele & Tramper, 2014).

Myoblasts have been used for culturing meat avoiding atrophy that can result in a large-scale uncontrolled growth of cells. Differentiation and proliferation of cells can be induced by mechanical, electromagnetic, gravitational, and fluid-flow methods (De Deyne, 2000). The repetitive contraction and relaxation can enhance the length of skeletal muscles by at least 10% (Powell et al, 2002).

One of the pressing unmet need for large-scale production of in vitro meat is to lower cost of culturing the cells (Mattick and Allenby 2010). The serum is highly expensive and needs to be used in substantial proportions to ensure significant cellular growth

To find low-cost alternatives, people have used serum-free media. An interesting recent development has been to use Cyanobacteria as a potential food source for cell growth. Cyanobacteria are photosynthetic bacteria with a protein content of up to 70% dry weight and can be easily cultured for large scale (Ford, 2011).

1.4 GLOBAL TRENDS

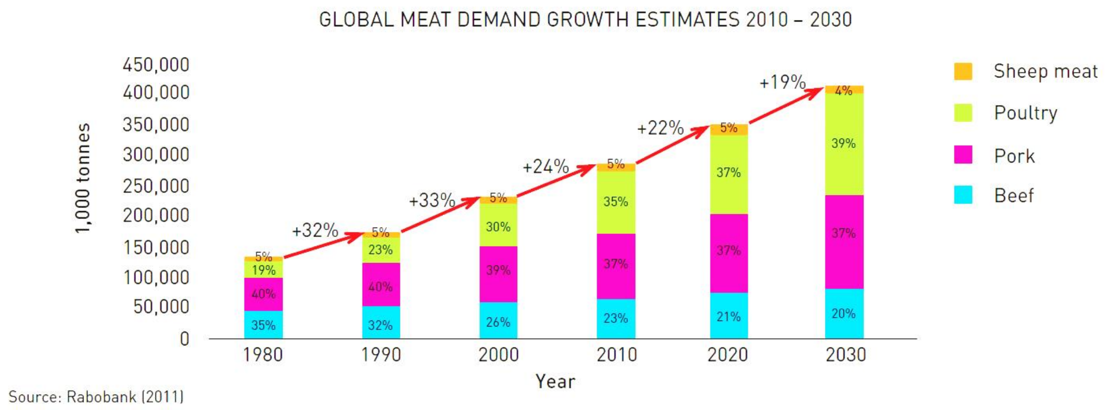
Estimates of when cellular agriculture products can reach grocery shelves are difficult to make, as their availability will depend on successful research and how well the regulations support them. With major advancements from a technology aspect, however, it is hoped that consumers will get to enjoy cultured meat products in the predictable future. Lab-grown or “cultured meat” could be a bridge between real meat and plant-based products.

30% of the calories consumed globally by humans come from meat products including beef, chicken, and pork. The meat industry has evolved into a complex global business that involves farms, middle-men, processing and storage centers, transportation, slaughterhouses and more. The commercial meat industry faces a rising tide of challenges in the form of business, ethical and environmental concerns. Meanwhile, start-ups using technology to engineer meat in labs or manufacture from plant-based products are rising in getting recognized and popularity. Meatless food products from beef-free burgers to pea based shrimp intimidate the future of the meat giants.

There are two non-profits funding and accelerating the research and commercialization of cellular agriculture: The Good Food Institute is donor-funded non-profit, which works to accelerate research and commercialization in this area. They work directly with universities and scientists to identify, fund, and write proposals for high-value projects, and are already working with a few labs in India. New Harvest is another research institute dedicating funds and efforts for the advancement of cellular agriculture. This donor-funded organization intends to solve major challenges coming on the road to commercialization that include finding a cost-effective medium for cell nutrition and developing an optimized bioreactor design (the machines in which cultured meat will be grown in larger quantities once production moves from the R&D stage in labs).

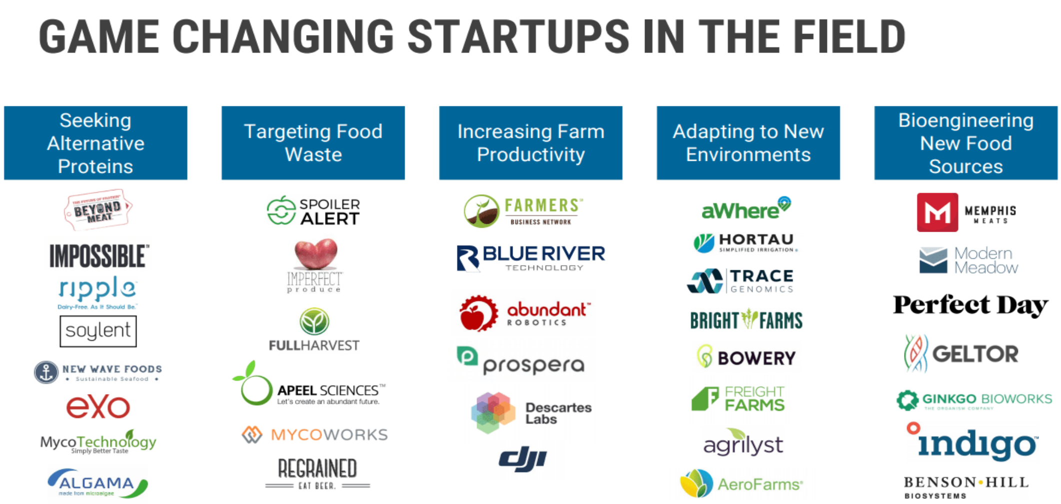
Some companies are competing and looking for avenues to launch their animal-free products first in the market of meatless space.Startup companies such as Hampton Creek and Memphis Meats hope to be the first ones to bring lab-grown meat to store shelves in 2018 and 20121 respectively.Taking a different approach, Yuki Hanyu, founder of Tokyo-based Integriculture and non-profit Shojinmeat Project, is working to acclimate future generations to a meatless future through open source tech.Hanyu is providing Japanese high school students access to high-tech heated boxes that allow them to culture animal cells at home and grow them into meat-like products.

San Francisco based Memphis Meats produces meat from self-replicating cells, thereby resulting in producing meat that is an "animal-based" product but avoiding the need to breed, raise, and slaughter huge numbers of animals.The company made public its first synthetic meatball in 2016 and followed up with the world's first cell-cultured chicken and duck earlier this year.Memphis Meats was not the first company to explore lab-grown meat products.In fact, Dr. Mark Post, a Netherlands-based researcher, produced the world's first lab-grown burger in 2013, in research originally financed by Google's co-founder Sergey Brin. This initiative resulted in MosaMeat, which aims to bring in vitro meat to market in the future.



http://www.chicken.org.au/industryprofile/page.php?id=2_Global_Context

Another company, Perfect Day is applying gene sequencing and 3D printing to create milk without the cow.Biotech companies are even exploring methods for engineering meat-like products from methane. While few companies are already developing methane-based animal feed, start-ups are now expressing interest in engineering methane-based protein fit for human consumption.California-based Calysta recently rose $40M in Series D funding, while India-based String Bio has received $100K from Future Food Asia to commercialize its technology.While protein products developed by these companies are not presently fit for consumption by humans, methane-based proteins could improve the environmental impact of meat production and eventually further ignite the meatless revolution by creating another food source for developing economies in Africa and Asia.



Source: www.cbinsights.com

Regulation is also starting to play a bigger role, as regulators explore cellular agriculture as a viable food source in the future.In March, the National Academies of Sciences, Engineering, and Medicine in Washington, D.C. released a report on the future of biotechnology developments and regulation, while the White House launched a review of how U.S. agencies regulate agricultural biotechnology.

As of now, artificial meat regulation is still in early stages. Regulatory responsibility could extend across multiple bodies and therefore become a complex procedure in an animal-free ecosystem, as e.g. biotechnology for food overlaps with many regulatory systems.

1.5 TIMELINE OF CELLULAR AGRICULTURE

Although cellular agriculture is a burgeoning and promising scientific discipline, cellular agriculture products were first commercialized in the early 20th century with insulin and rennet. Winston Churchill also predicted the advent of a mainstream cellular agriculture concept of meat production in his 1931 essay, Fifty Years Hence.

"Fifty years hence...we shall escape the absurdity of growing a whole chicken in order to eat the breast or wing, by growing these parts separately under a suitable medium."

Things went quiet until in 1991, a U.S. researcher Jon F. Vein secured a patent (U.S. Patent 6,835,390 B1) for the production of tissue engineered meat for human consumption. The patent included the technique where muscle and fat cells grow in an integrated fashion to create food products such as beef, poultry, and fish. In 2001, WieteWesterhofa dermatologist from University of Amsterdam filed a worldwide patent on a process to produce cultured meat (Sandle. T. 2017).

In 2004, Jason Matheny founded New Harvest which was first a cultured meat promoting organization but whose mission is now to "expedite advances in cellular agriculture."New Harvest is the only organization focussing exclusively on publicizing the field of cellular agriculture and are funding the first cellular agriculture Ph.D. at Tufts University.

Since 2014, IndieBio, a synthetic biology accelerator in San Francisco, has incubated several cellular agriculture start-ups, hosting Muufri (making milk from cell culture), Clara Foods (making egg whites from culturing cells), Gelzen (making gelatin from bacteria and yeast), Affineur (making cultured coffee beans) and Pembient (biofabricating rhino horn). Muufri and Clara Foods were both floated by New Harvest.

In 2016, the Good Food Institute (GFI) was founded to promote and accelerate the commercialization and research of alternatives to animal agriculture, including plant-based meats and clean meat. GFI works with universities, startups, meat producers, governments, and others to invest in this area.

Below mentioned graphical representation brings out the important events and researches related to Cellular agriculture:

TIFAC (DST) organizes a national debate on "Cellular Agriculture" on its 31st Foundation Day and publishes a policy document	**2018**	
	2018	White Paper on Meat: The Future brought out by World Economic Forum on 23rd January 2018
Bay Area start-up Memphis Meats declares the development of the world's first chicken strip grown from self-reproducing cells	**2017**	
	2016	New Harvest hosted the first-ever global cellular agriculture conference
Memphis Meats announces the creation of the first in vitro meatball	**2016**	
	2016	The Good Food Institute, an organization dedicated to promoting alternatives to animal food products - including cellular agriculture - is founded
According to Mark Post's lab, the cost of producing an in vitro hamburger patty drops from $325,000 in 2013 to less than $12	**2015**	
	2014	Modern Meadow presents "steak chips", discs of lab-grown meat that could be produced at a relatively low cost
Real Vegan Cheese, a start-up aimed at creating cultured cheese is founded	**2014**	

	2014	Muufri and Clara Foods, companies aimed at producing cultured dairy and eggs, respectively, are founded with the assistance of New Harvest
The first in vitro hamburger, developed by Dutch researcher Mark Post's lab, is taste-tested	**2013**	
	2011	The company Modern Meadow, aimed at producing cultured leather and meat is founded
People for the Ethical Treatment of Animals offers a $1 million prize to the first group to make a commercially viable lab-grown chicken by 2012	**2008**	
	2008	The In Vitro Meat Consortium holds the first international conference on the production of in vitro meat
Dutch government agency SenterNovem begins funding cultured meat research	**2005**	
	2004	Jason Matheny founds New Harvest, the first non-profit to work for the development of cultured meat
Researchers culture muscle tissue of the common goldfish in Petri dishes. The meat was judged by a test-panel to be acceptable as food	**2002**	
	2001	NASA begins in vitro meat experiments, producing cultured turkey meat
Willem van Eelen secures the first patent for in vitro meat	**1999**	
	1995	The U.S. Food and Drug Administration approves the use of commercial in-vitro meat production
Russell Ross achieves the in vitro cultivation of muscular fibers	**1971**	

1.6 INDIAN TRENDS

India is often thought of as an all-vegetarian country, but over 70% of India is non-vegetarian. About 300 Crores Chickens and 8 Crores Goats are slaughtered each year in India.

Currently, there is not much happening within the space of lab-grown meat. The recent TIFAC event (2018) at IIT Delhi on the next food revolution, brought together scientists, businessmen, policymakers, politicians, religious leaders on a common platform to discuss various aspects of cellular agriculture. This has generated significant interest and set a fertile ground for the future generation of innovators, investors, and regulators.

From an Indian perspective, a step from the private sector has been taken in this direction. Ahimsa Food is the first company to go into 'Mock Meat' production in the country. It produces gourmet Vegetarian food and has named its brand 'Veggie Champ'.India based String Bio has received $100K from Future Food Asia to commercialize its technology of developing methane-based animal feed.

1.7 PATENT ANALYSIS

As it is clear from the information mentioned above, the cellular agriculture technology is used for not only meat, eggs or milk, but also for leather, perfumes, and silk as well. The patent search was conducted using different synonyms of meat, leather, egg, milk, silk, fragrance specifically in the context of cellular agriculture. The synonyms used in the search of meat were muscle, flesh, red meat and for milk other terms used were beta casein milk protein, kappa casein. Similarly, egg white protein, yolk, cholesterol was used in place of an egg; collagen, protein, hide, skin for leather; silk protein, protein fibres for searching patents for silk and perfume, aroma, scent, essence, incense in place of fragrance. The search string was made using these synonyms with other keywords like artificial, cultured, in-vitro, synthetic, tissue-engineered, bioengineered, recombinant and transgenic and then applying Boolean operators and wildcard characters for modifying the search. These were then made into a search string and a search was done in different databases.

The patent search was carried out in both paid and free databases - United States Patent and Trademark Office (USPTO), PATENTSCOPE, Indian Patent Office (IPO), ESPACENET, Global Patent Index (GPI) and National Knowledge Resource Consortium (NKRC). Both keywords search and IPC search was carried out. The IPCs were picked from the relevant patents that were obtained in search results.

All the patents were exported into an excel sheet and duplicates were removed. There were 694 documents obtained after removing the duplicates. Abstracts and claim for all of these were read and analyzed. Only 5 patents were found to be relevant to milk. Similarly, 40 patents were found for meat, 3 patents for fragrance, and one patent each for silk, egg, and leather respectively.

In a nutshell, documents retrieved through patent searches through keywords and IPC were 51 to be relevant to cellular agriculture specifically in the context of cellular agriculture technology based meat, milk, egg, silk, leather, and perfumes.

However, it is important to note that there is a long history of translational R&D, which effectively provides the clean meat field with an accelerated path to commercialization. Decades of research and investment in relevant fields like stem cell biology, developmental biology, and cell-based therapeutics have enabled a detailed understanding of the thebasic biology underlying the growth and differentiation of cells outside their native animal systems. (Specht, ‘Is the Future of Meat Animal Free?', 2018)

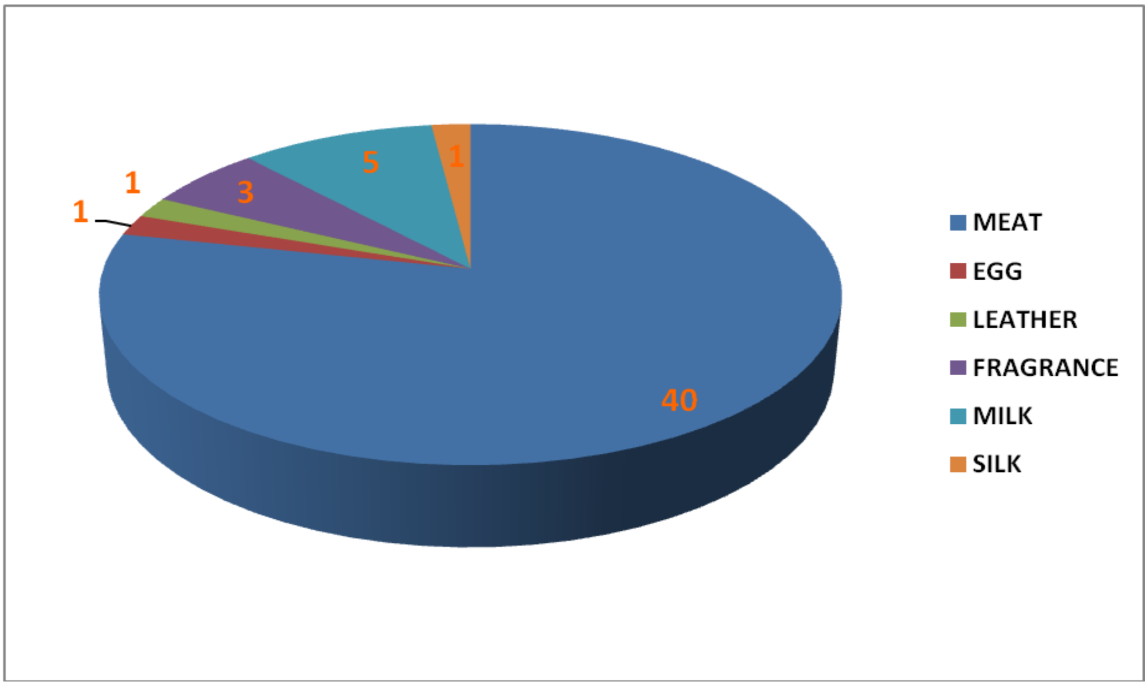


Figure **1**- No. of patents in relevant fields

Then backward and forward citation search was conducted only for four categories of products namely meat, egg, leather, fragrance. All the patents were exported into an excel sheet and duplicates were removed. In total 116 patents/applications were found to be relevant to cellular agriculture for above-mentioned four products.

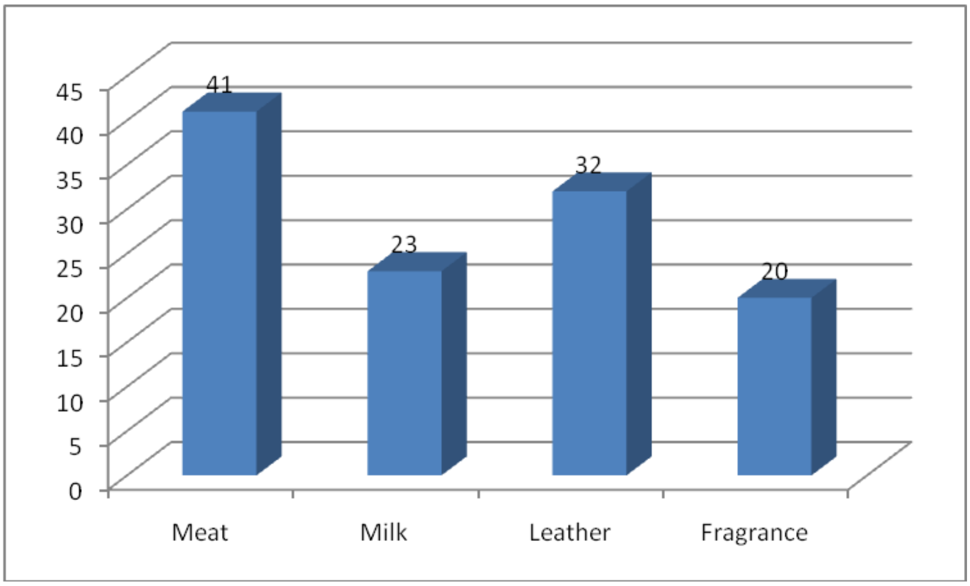


Figure **2**- No. of Patents after the backward and forward citation

The major IPCs are A23J, A23K, A23L, and A23C which includes live microorganisms, Meat products; Meat meal; Preparation or treatment thereof, Working-up of proteins for foodstuffs, containing or treated with, microorganisms, enzymes, or antibiotics. Another important IPCs is A63K which includes Fat tissue; adipocytes; stromal cells; Connective tissues. The other IPC is C12N and C12P which includes Bacteria; Culture media, therefore, preparation of peptides or proteins and aromatic.

(a) Key players

While doing a patent analysis, one of the important parameters to be considered is the size of the IP portfolio of the leading entities or technology players in the area. Top eight players were determined. Impossible Foods, Beyond Meat, and Modern Meadow came out to be the key players with.16, 16, 14 patents each respectively. They are closely followed by Memphis Meat, Clara Foods, Perfect Day, Bolt Threads, and Gingko Bioworks.

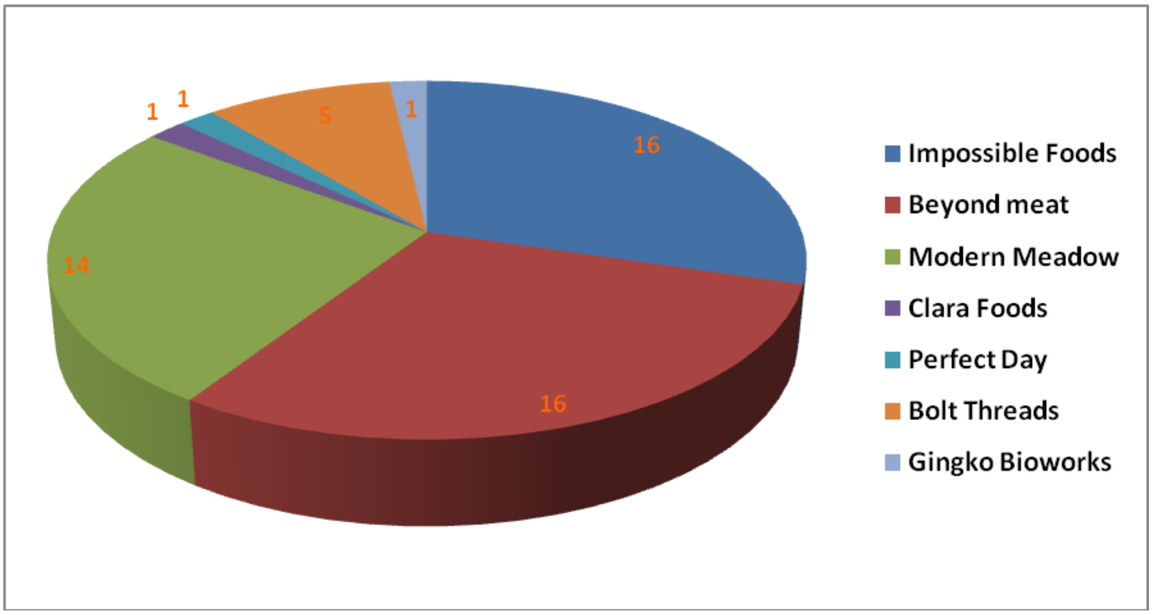


Figure 3-Major players commercializing cellular agriculture-based products

(b) Important Patents

There are many patents which relate to the cellular agriculture or played an important role in the evolution of the cellular agriculture. Important patents of covering different aspects of cellular agriculture are discussed below:

1) Title: Methods and Compositions for egg white protein production

Applicant: Clara foods and Company, USA

Application numbers: WO2016077457-A1; EP3217807-A1; CN107205432-A; JP2018501814-W

Abstract: Method of producing egg white protein composition, involves recombinantly expressing egg white proteins and mixing the two or more egg white proteins. The method is useful for producing egg white protein composition which is useful for preparing processed consumable product (all claimed) including food products, beverage products, dietary supplements, food additives, pharmaceutical products, and hygiene products. The method produces an egg white protein composition which has excellent metabolic stability and in vivo half-life, and produces an egg white protein composition which is used in reduced dosage.

2) Title - Non-dairy cheese replica

Applicant: Impossible food Inc, USA

Application numbers: WO2013010037-A1 ; AU2012281064-A1 ; CA2841470-A1 ; KR2014046462-A ; US2014127358-A1 ;

Abstract: This patent is an important patent as it gave lead for cellular agriculture milk related products as it was filed for a patent in different countries - China, Europe, USA, Canada, Korea, Japan, Australia, Mexico, India, Russia, Brazil and Hong Kong.

This patent describes methods and compositions for the production of cheese replicas. Generally, the cheese replicas are produced by inducing the enzymatic curdling of non-dairy milk.Making a non-dairy cheese replica comprises: either preparing an emulsion comprising proteins and fats from plant sources, inducing the emulsion to form a gel by enzymatic crosslinking of the proteins or denaturing the proteins, and producing a cheese-replica from the gel; or decompounding nuts or seeds in water, removing at least 85% of the suspended solids and adding a transglutaminase to catalyzes the formation of crosslinks between proteins from the nuts.The method is useful for making non-dairy cheese replica. The method is capable of economically, making non-dairy cheese replica with less time-consuming. The cheese replica has improved properties such as hardness, cohesiveness, brittleness, chewiness, gumminess, viscosity, elasticity and adhesiveness.

3) Title: Methods and Compositions for Consumables

Applicant: Sand Hill Foods Inc

Application numbers: WO2013010042-A1 ; AU2012281069-A1 ; CA2841473-A1 ; KR2014047125-A ; AU2012281069-A2 ; EP2731446-A1 ; US2014193547-A1

Abstract: A meat substitute composition comprises a protein content, where one or more isolated and purified proteins account for 10% or more of the protein content by weight, where the meat substitute composition accurately mimics the taste, texture, or color of a meat product derived from animal sources. The meat substitute composition is useful for making muscle tissue replica, fat tissue replica, and connective tissue replica (all claimed). The invention provides improved methods and compositions which more accurately replicate the characteristics that consumers value in the preparation and consumption of meat and which overcome the shortcomings and drawbacks of current meat substitutes.

4) Title: Reinforced engineered biomaterials and methods of manufacture thereof

Applicant: Modern Meadow Inc, USA

Application number: WO2016073453-A1; EP3215670-A1

Abstract: This patent application is a method of leather production by cellular agriculture.Method for making reinforced engineered hide, involves (i) placing a first several collagen-releasing cells on a first surface of a mesh, (ii) culturing the first several collagen-releasing cells to form a first layer of collagen covering the first surface, (iii) flipping the mesh over and placing a second several collagen-releasing cells onto the second surface of the mesh, and (iv) culturing the second several collagen-releasing cells to form a second layer of collagen covering the second surface. The method is useful for making reinforced engineered hide. The method is also useful for forming a fiber-reinforced biological tissue composition.The reinforced engineered hide has superior durability and flexibility compared to other engineered materials and native leather and enables to retain the look and feel of native leather.

5) Title: Cymbopogon citrates fragrance-producing endophytic bacterium

Applicant: Hunan University, China

Application number: CN201410278532

Abstract: This Cymbopogon is being used by many patents filed in China by Chinese applicants for bacterial production of fragrance.The invention discloses an endophytic bacterium pantoea sp. CcSh-1 generating volatile fragrant substance, and the preservation number is CGMCCNo.8715. The bacterial strain comes from the sheath part of matured cymbopogoncitratus, is easy to culture, and is capable of generating refreshing and pleasing fragrance after being grown on a solid medium for 2-3 days, and the fragrant substance is identified to contain a citral composition. The bacterium provides a new microbial source for replacing plant raw materials producing perfumes.

6) Title: Methods and compositions for synthesizing improved silk fibers

Applicant: Bolt Threads Inc

Application number: US 2014056117 W 20140917 (EN)

Abstract: The present disclosure provides methods and compositions for directed to synthetic block copolymer proteins, expression constructs for their secretion, recombinant microorganisms for their production, and synthetic fibres (including advantageously, microfibers) comprising these proteins that recapitulate many properties of natural silk. The recombinant microorganisms can be used for the commercial production of silk-like fibres.

Conclusions of Patent analysis:

Foundation for cellular agriculture was done in 1912 by French biologist Alexis Carrel and then expanded in different countries mainly in Israel, United States of America, and Netherland. Among these three countries USA is the major producer of cellular agriculture related products.

Cellular agriculture is divided into two categories food and material. Artificial meat leads the food group with maximum number of patents filed in this area and eggs the least number of patents filed. Fragrance is leading the material group with maximum number of patents filed and Silk the least.

The patent analysis shows that the major push for cellular agriculture came with the invention of recombinant technology and patents filed in seventies. US patent 5298422 entitled "Myogenic vector systems" filed on Nov 6, 1991 is the milestone patent filed by Baylor College Of Medicine with Robert J. Schwartz, Franco J. DeMayo, Bert W. O'Malley as inventors. This invention was supported by a grant from the United States government under HL-38401 awarded by the National Institute of Health. This important invention was followed by few inventions filed under the title "Tissue engineered meat for consumption and a method for producing tissue engineered meat for consumption" by the inventor Jon Vein filed from 2002 onwards. There after researchers started further work in cultured meat, silk, milk, fragrance, leather and egg. Presently, world has started accepting the cellular agriculture trend. Major key-players Impossible Foods, Beyond Meat, and Modern Meadow based in USA are developing their techniques for more acceptable food and other cultured materials.

1.8 CHALLENGES

Emotional: Any disruptive technology is bound to create turbulence in the existing practices. Consumer acceptance will come after prolonged experience and word of the mouth of what goes into the mouth. The key is to make it appear natural in terms of its looks, taste, texture, and flavor (Post 2012). Large-scale consumer studies have not yet surfaced due to nonavailability of such food in the market. However, initial data has indicated mixed reactions.Of the studies which were found to have representative samples, Wilks and Phillips (2017) give an overall positive view of consumer acceptance, reporting that 65.3% would be willing to try cultured meat, of whom 32.6% would be willing to eat it regularly, 47.7% would be more willing to eat it compared to soy-based meat substitutes, and 31.5% would be willing to eat it as a replacement for farmed meat.On the whole, more studies are needed, in order to gain a wider understanding of the consumer acceptance of clean meat. Various countries have initiated public surveys to find the bottleneck issues and resolve them for mass acceptance. The cultured meat may sound unnatural and unappealing for some, exciting and exploratory for some. The Good Food Institute currently has a cross-cultural survey underway in the US, China, and India, which will return data on consumer acceptance of clean meat, and how it may be affected by cultural context.

Despite technical advances, consumer acceptance of eating petri plate grown meat is still a relatively unexplored space. Perhaps if the cost of producing lab-grown meat comes down than the current prices of obtaining meat from natural sources, the technology, and the lab-grown product might find resonance in an economically distressed section of the society. Likewise, people with exploratory nature might find in vitro meat a new sensory experience. Given that food has not only nutritional but also emotional value, we may find acceptance based on the personal definition of ethical and popular. Sometimes statements like "Cultured meat is unnatural, and thus unhealthy/ dangerous/undesirable" comes from the knowledge that is partial and may be biased.

Many consumers face a psychological barrier towards eating lab-grown foods and may prefer the familiar taste of real meat products. While groups like aforementioned Shojin meat Project are acclimatizing future consumers to cultured meat, socialization will need to happen on a global scale.

(b) Technical issues: As mentioned, there are four critical technology elements, which require research and development, to create cost-competitiveness at scale: cell lines, nutrient media, scaffolds, and bioreactors. Standardizing meat culture, regarding source and process, is a major challenge. Stem cells might be preferred by some. However, contamination and retention of stem cell property can be a major challenge. Currently, culture media used to grow stem cells is quite standardized and comes with fetal bovine serum. In future, as the community moves towards serum-free media, finding a new growth medium and protocol for culturing stem cells, would be a pressing need. For example, people are trying to use cyanobacteria hydrolysate or other vegetarian supplements like coconut water. But so far, the industry has not accepted alternative cell culture protocols. With more research, it may be eventually possible to grow cells in serum-free media on a commercial basis. However, developing muscle fibers along with other hard and soft tissue remains a major challenge.

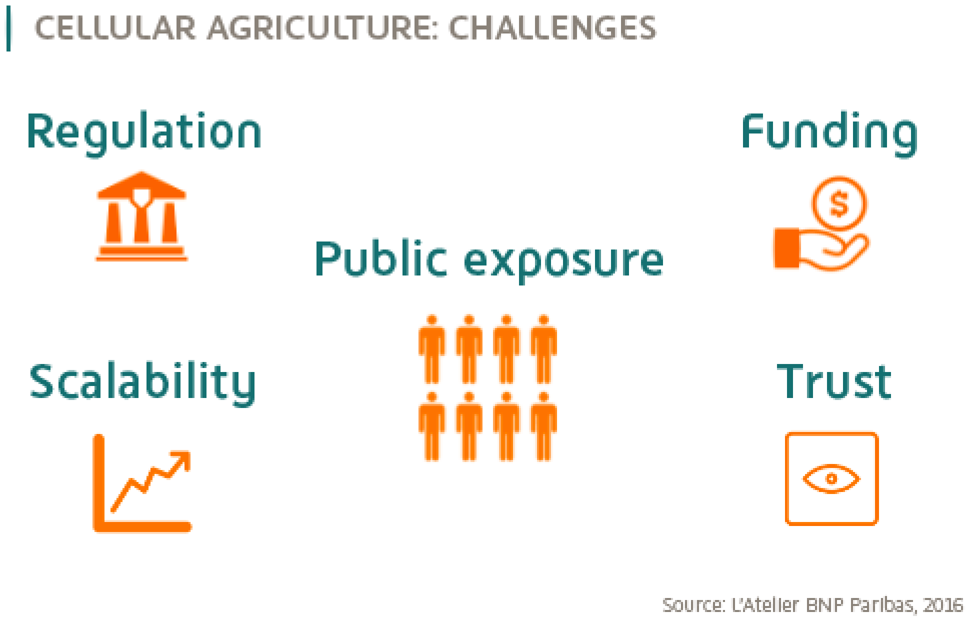
To bring in acceptance, the natural pigment myoglobin needs to be expressed by cultured cells to give it a reddish color. Creating nature's equivalent of meat in the lab is a huge challenge because we not only need blood and muscle to give the border an authentic look but also fat derived and water-soluble components that give it a meaty flavor. Some companies dip steak pieces in a special sauce before dehydrating the mass, to give additional flavor.

(c) Environmental impact: According to the United States Environmental Protection Agency, the livestock industry is the primary emitter of methane, a greenhouse gas 25 times more powerful than CO_2. It also uses 26 percent of the world's land for grazing and causes 80 percent of deforestation in the Amazon rainforest region. Although the users are expressing great interest in cultured meat, there are many hurdles which must be overcome through further scientific research to make the products reach the market.It is unclear that meatless products would be better for the environment. Despite claims that less meat consumption will reduce environmental impact, lab-based technologies can come with their own baggage of high costs for electricity, heating, and other resources.

(d) Cost of clean meat: In the current form, the process is expensive and it takes a long time for scientists to produce the meat. One of the main reasons that lab-grown meat is so expensive is due to the occurrence of fetal bovine serum, or FBS, in meatless products. FBS, which is extracted from cow fetuses, is a main and costly ingredient in lab-grown meat. However, start-ups are looking to do away with the use of FBS from the meatless equation, in order to cut costs. Just has reported that it has developed a method to grow cell cultured chicken without FBS, while Memphis Meats is validating methods to produce its meats without the ingredient.But once an alternate source replacing FBS is established, it would definitely make the cellular agriculture-based products to be better accepted by people especially vegetarians.

Commercial production of products through cellular agriculture specifically clean meat is challenging. Though many start-ups in the meatless space claim that their products will drastically transform meat consumption, the question remains whether clean meat will provide a scalable method to feed the future. Aforementioned cost considerations are crucial in scaling these products for mainstream consumption. But as with the computers, cell phones the technology became more efficient as it progressed and similarly, there will come a day when we see lab-grown agricultural products based on cellular agriculture line up in our grocery store shelves.Moreover, The number of prototypes, demonstrations, and tastings in the last two years indicate that there are no fundamental technological flaws that are prohibitive to the feasibility of the endeavor. As clean meat comes to fruition, the main challenges for cost reduction will reside in scale-up, with an abundance of opportunities within each critical technology element to increase the efficiency of the process and continuously decrease the cost. (Specht et al, ‘Opportunities for Applying Biomedical Production and Manufacturing Methods to the Development of the Clean Meat Industry', 2018)

(e) Legal: Any new technology must consider the legal issues raised by branding or manufacture of its products before being able to bring the products to the market as current laws and regulations are not drafted with this industry in mind. The Good Food Institute which is a clean meat non-profit based in the United States is working in the direction to document the regulatory requirements in different countries. Recently a white paper which is going to serve the platform for the final paper expected to be brought out by World Economic Forum in 2019 has been drafted. This short paper aims to help accelerate the agenda for change and to stimulate new ideas and collaborations for global meat production and wider protein delivery.



The automation of meat production industry could have far-reaching job implications for the agriculture industry. The meat sector is the largest employer within US agriculture and mainstream meatless consumption could create chaos and reduce jobs across the entire meat production value chain. However, if the in vitro industry becomes popular and less expensive, we might see surges of employment opportunities in new areas.

(f) Health impacts: Health risks vary and are also dependent upon an individual genomic constitution that has a unique way to interact with the environmental inputs. Overall, the human health impact of the current livestock meat practices may be viewed as issues of composition and infection.

The meat composition issue has been highlighted repeatedly in the past in many surveys and is now well established that saturated fat and cholesterol that generously find their way into the human alimentary canal in the fast food outlets are bad for health.

The risk of diseases arising from consumption of meat (from natural livestock) may lead to atherosclerosis, diabetes, Cardio Vascular Diseases (CVD) and cancer. Cultured meat can come handy in this space, as one can regulate the nutrients e.g., it is possible to control the ratio of omega 6 and omega 3 fatty acids (Williams 2012) to create a healthier meat. It has been found that meat originating from poultry farm is at a significant risk of infection and transmission of this infection to humans. According to the World Health Organisation ‘Campylobacter species are now the commonest cause of bacterial gastroenteritis and predominantly associated with consumption of poultry'.Data suggest that approx. 90 % chickens in US and 50–75 % in the UK are infected with Campylobacter.

Trichinosis (an infection caused by the roundworm Trichinella spiralis, leading to diarrhea, abdominal cramps, muscle pain, and fever) can be acquired if people eat raw or undercooked contaminated meat. The etiology of diseases like Bovine Spongiform Encephalopathy (BSE), Swine flu and Foot and mouth disease (FMD) have animal origins and clearly established. It is a common knowledge that livestock meat industry practices rampant use to antibiotics and other hormones to promote the growth of tissue and prevent infection. These chemicals find an easy way into the human food chain and generate more health problems. Finally, in many countries, cattle are fed with low-quality food and left to graze randomly. Due to this reason, they all kinds of toxic substances find a way into cattle biomass and eventually humans.

1.9 MERITS

Global meat production is expected to nearly double to 445 million tonnes by 2050in comparison to what stands today i.e. 263 million tonnes and (Nierenberg D, 2003). This represents a factor of ten rises from 1960 to 2050. Over the same period, the global population is expected to triple from roughly 3 to 9 billion people. There are significant environmental consequences from today's global meat production, as recent research sponsored by the Climate and Land Use Alliance shows (CLIMATEFOCUS, 2017). According to the FAO, livestock generates just under 15% of the total CO2 equivalent greenhouse gas emissions a year, with beef cattle alone contributing about 6% of the global total – an equivalent of about three times that of the aviation sector (IATA. 2009). Researchers also calculated that it can take about 15,000 litres of water to produce a kilo of beef (Mekonned, M.M. and Hoekstra A. Y., 2010) – a challenge exacerbated when key livestock production regions such as the south-west United States and south-west Brazil and other regions dependent on livestock production for exports such as India and Australia are facing enhanced frequencies of drought and subsequent water stress.

Additionally, meat production is a major driver of deforestation, habitat and biodiversity loss, through conversion of natural landscapes to pasture lands and agriculture for feed production. World Health Organization is concerned about the spread of microbial resistance due to the overuse of antibiotics for managing livestock.

Considering all of the above, Cellular agriculture is an important and perhaps revolutionary, technology that presents opportunities to improve animal welfare, enhance human health, and decrease the environmental footprint of meat production. Removing our dependence on animals for agricultural products can significantly reduce antibiotic overuse on livestock, and provide a sustainable way to feed a population of over 9 billion by 2050. Cellular agriculture may also open the door to new and safer gastronomic possibilities.

Moreover, meat production is unsustainable and will not be able to meet further meat demands if it continues with current techniques. That's why we need cellular agriculture to fulfill our meat demands while reducing its impact on the environment.Animal culture right now is extremely detrimental to animals, human health, and the environment.

1.10 FUTURE

Much of the biotechnology research needed to mass produce cultured meat has yet to be matured, including studies on optimal cell lines and culture media. Furthermore, there are no scientific disciplines, departments or institutes devoted entirely to the research on "bio-fabrication" or "cellular agriculture"

https://guestlist.net/article/92758/lab-grown-meat-is-the-future

Most research in the space of lab-grown meat is individual investigator-driven as exploratory projects and have not witnessed widespread academic interest. The cellular agriculture sector will see a booming contribution from academia if there are assured funding by the government. Though some countries have taken the significant and early lead in this area, there is a general lack of regulatory preparedness. It is unclear whether the cultured meat will be considered a natural extension of raw meat or genetically modified food. There needs to be a discussion along regulatory lines to alleviate any concerns that may arise in due course.

The mimicry of the natural products in the form of hamburger and meatball may be technically successful. However, more research is required to make them meaty and customize moisture, fat, taste, texture and nutritional composition.

Although prototypes of animal-free culture media exist and have been used to produce muscle tissue, more research is required to find optimal cell lines for large-scale meat production using generic media that is easy to procure, comes from non-animal sources and can sustain a large-scale culture in bioreactors. Microalgae, as a rich source of nutrients, has been explored. However, challenges remain about their large-scale production and customized use for meat production vis-à-vis their use for making biofuels and animal feed

A less discussed issue is the high energy requirements that cellular agriculture industry demands for sustained production of cultured meat. There is a need to conduct studies to understand cost to benefit ratio in the emerging area of cellular agriculture.

Currently the cost of making meat balls or burgers are exorbitant and beyond the reach of a large section of the community. Research is required to find innovative ways to grow cells, lower the cost, find cheaper nutrient sources and automate the process, wherever possible. Government may also consider subsidizing of cellular agriculture to ensure large scale participation and benefits to economically less fortunate sections of the society.

Lab-grown meat has generated a massive hype in the media, resulting projections of the current progress that may not be real. The high-intensity media buzz may create novel sources of funding and public debates, but it is essential to have a realistic estimate of the current situation, present pros and cons of the emerging industry, leave sufficient space and time for fundamental research to develop credible and lasting alternatives to livestock farming.

Compared to the conventionally produced meat, cultured meat involves 78– 96 % lower greenhouse gas emissions, 99 % lower land use and 82– 96 % lower water use. Recent studies have indicated two orders of magnitude reduction in the land and water use by switching from livestock production to lab production (Tumisto and Roy 2012).

Cultured meat can eliminate the suffering of animals while satisfying nutritional and emotional requirements of meat eaters (Holmes & Decay, 2008). By culturing meat, one can control meat composition and quality by modifying flavor, fatty acid composition, add health boosting and functional ingredients to the meat (Van Eelen, 2007).

The first "In vitro Meat Symposium" held in Norway (2008), generated a prediction that the first commercial in vitro meat products would be available for the public in the next 5 to 10 years at competitive prices. The animal to human disease transmission can be curbed, environmental carbon dioxide and methane gas content brought down significantly, reduce the massive waste nitrate released from cattle farms, offer a safe, nutrition and affordable meat, reduce food shortages

1.12 CONCLUSIONS

Cellular agriculture offers an excellent promise to the society, eliminates atrocities on animals, reduces the disease burden on humans, reduce environmental damage that livestock farming causes. The era of victimless meat has already arrived. Animals need to be treated with love and care. We need to see animals as essential part of our society than satisfying our hunger on the dining table.

https://www.theguardian.com/science/2013/jan/05/the-future-of-food

By some estimates, 30% of the calories consumed globally by humans come from meat products, including beef, chicken, and pork. Estimates of when cellular agriculture products can reach store shelves are difficult to make, as their availability will depend on successful research. With significant advances, however, it is expected that consumers will get to enjoy cultured meat products in the anticipated future. Irrespective of the hurdles to a meatless future, clean meat products are diversifying, growing and attracting investors & public attention alike.

Realizing positive outcomes on all fronts will require technologists, policymakers, and individual consumers to understand this technology and make wise, well-informed decisions as it is developed. If monitored and managed appropriately, cellular agriculture could allow humans to produce more food with limited resources while simultaneously mitigating other environmental problems.

Cost and scale are immediate considerations in moving these products from unique and innovative purchases to everyday kitchen staples. In the next few years, it can be likely expected to see the cost of lab-grown meat decrease considerably. Constant advances in genetic engineering and plant-based innovation will augment taste, flavor, and health benefits to the products. These technologies will also continue to expand across the categories of untouched meat and seafood (e.g. pork, duck, eel, etc.).

In coming future, the meat value chain could be simplified dramatically, as the clean meat lab or factory could replace the farms, feedlots, middle-men, processing and storage centers and slaughterhouses. Also, users or consumers will need to adjust their mindsets to accept the products developed from new technology for the betterment of the planet.

… But a truly meatless future has challenges to overcome and get a due place in our kitchen.

1.12 RECOMMENDATIONS

As mentioned, the technical talent and impetus exists in India, to invest in the space of cellular agriculture, and meaningfully influence its growth on a global scale. Indian industry, government, and research institutions can play a role in bringing the commercialization of clean meat close to reality. The Government of India already has some programs and initiatives which may be applicable for such an endeavor, including the Institutes of Eminence initiative, Prime Minister's Research Development Fund, BIRAC BIG Grants, ICAR-NAARM technical training, etc. Additionally, the Indian biomedical industry already has the innovation, expertise, and scale which would be required to make clean meat cost-competitive with conventional meat. For example, Biocon, India's most valuable biotech company, is also one of the world's largest manufacturers of insulin by volume; similar processes and inputs (growth factors) used to manufacture insulin, can be applied to cellular agriculture.

The pre-competitive nature of the clean meat landscape means that there will need to be a lot of co-operation and strategic coordination among all parties to enable forecasting of long-term hurdles. The following areas may be earmarked as broad categories of initiatives, which may be pursued to push cellular agriculture forward in India:

1. **Seeding research & development:**

As indicated, this is an area which will require participation from government funding, research institutes, and universities and corporate entities which may include biopharma companies. Specific initiatives may be pursued which could consist of:

- In conjunction with expert organizations such as the Good Food Institute and New Harvest, identification of the highest priority research projects which may be undertaken by scientists at elite Indian institutions such as ICT Mumbai and CCMB

Hyderabad. These priority projects may be supported by grants and joint proposals to large foundations. Department of Science & Technology (DST), Department of Biotechnology (DBT) and other government and civil organizations, such as the Association of Food Scientists and Technologists (AFST), may be tapped for the same. These high-priority projects may be put out in the form of a Request for Proposals (RFP) by researchers, to increase the volume of high-impact publications in this area.

- Creating a researcher database by assessing the top research institutes in the country, and identifying the most promising labs and researchers to take on these projects, by equipment, credentials, publications, etc. This database may be used to fast-track funding such as DBT grants, to the most promising labs and researchers.
- The establishment of Centres for Cellular Agriculture at top research institutes such as CCMB. These could be funded through government grants such as the Institutes of Eminence program, in conjunction with large private donors and foundations.
- Creating a consortium of public and private entities, including large pharma companies, to perform direct research. This research may be held in the form of joint IP amongst the entities involved. This would be a similar model to consortiums already being assembled in Israel and other markets, including government, large corporate entities, universities, and startups.
- Creating specialized grants for cellular agriculture among the earmarked funds for Biotechnology Ignition Grant (BIG), Prime Minister’s Research & Development Fund (PMRDF), as well as prizes for the best proposals to be funded at the university level.
- Working directly with foundations such as Rockefeller Foundation, Gates Foundation, and governments such as the Israeli government, which have all demonstrated a record of funding research and commercialization of social technologies, to increase investment in this area.

2. **Technical talent:**

One crucial area of advancement to build the ecosystem for cellular agriculture is the bottleneck of technical expertise which is well versed in these areas. As cellular agriculture is a specialized area, but one who benefits from translational R&D and knowledge from tissue engineering, biopharma, and cell-based therapeutics, it is entirely possible to train talent in these areas to be applied to cellular agriculture. Some initiatives which may be undertaken include:

- Creating a co-operative working group with ICAR, ICAR-NAARM, MHRD Department of Higher Education, and other relevant bodies, to note how education and continuing education curriculum for engineers, scientists, and food technologists, could be supplemented to include cellular agriculture modules.
- Working directly with universities to create courses in synthetic biology and cellular agriculture. For example, the Good Food Institute and the University of California, Berkeley had together created the world's first course solely focussing on developing plant-meat products. It is now part of the new 'alt.meat lab' for engineering, science, and entrepreneurship students to utilize high-tech approaches to create plant-based meat alternatives targeted at satisfying meat lovers. Similar dialogue is underway with Jawaharlal Nehru University in Delhi, to develop synthetic biology courses for clean meat production.
- Sponsoring technical talent to attend international conferences where there is an exchange of ideas regarding the cutting edge technologies in the context of cellular agriculture. For example, the New Harvest Conference (July 2018), and the Good Food Conference (September 2018). These events host speakers and attendees from the leading companies in clean meat, including Memphis Meats, Mosa Meats, JUST/Hampton Creek, etc. It would be invaluable for our scientists to spend some time in this company.

3. **Supporting Industry and Entrepreneurs:**

The government and private funders should be equally involved in creating the conditions necessary for commercialization of these technologies, given that they represent a transformational potential for the food system. It is essential to ensure that there is coordination between research entities and those involved in commercialization. As mentioned before, to leverage funding most efficiently across the entire technology readiness level (TRL) development of this industry, a concerted effort to bridge the gap between academia and industry is needed. Developing academic/industry collaborative consortia is one approach to ensure that early-stage research is performed with large-scale manufacturing considerations at the top of mind, thus positioning industry partners at the receiving end of successful research outcomes. Facilitating robust dialogue among all the stakeholders, including contracted researchers, vendors in life sciences, and the clean meat companies themselves can de-risk investments in this space by reducing duplicative effort and maximizing the licensable opportunities for intellectual property (IP) that is developed by each clean meat company. Models for pooling IP or establishing patent pledges that reduce the risk of litigation have proven successful for fostering open collaboration in other fast-moving, disruptive technology sectors. (Specht et al., 'Opportunities for Applying Biomedical Production and Manufacturing Methods to the Development of the Clean Meat Industry', 2018) Some indicative activities in promoting commercialization could include:

- Providing for cellular agriculture as a specific area of incentives in Invest India and Make in India initiatives. (Currently, the Make In India framework lists biotechnology and food processing separately, but not cellular agriculture.) This would result in the growth of Indian startups tackling this area, as well as foreign direct investment (FDI) from companies who are already working in this space. For example, the leadership of JUST, Inc (formerly Hampton Creek) has already indicated their desire to set up a manufacturing hub in Asia. India is an attractive market for this under the initiatives of the government.
- Creating robust mechanisms for intellectual property filing and protection, particularly at the level of startups. Filing for patents is an expensive process. Strengthening the education system for intellectual property law, in general, will have a direct effect on the resources available to people in business in cellular agriculture.
- Establishing and strengthening incubators such as Agri BioNest and Agri Udaan. These are unique public-private partnership organizations which receive funding from DBT and operational expertise from NAARM, and private partners (Caspian).
- Private investment and promotion in cellular agriculture. As outlined earlier, in other markets such as the United States and Europe, investors and private industry such as DFJ, NewCrop Capital, Temasek, Bill Gates, Richard Branson, Cargill, Tyson Foods, etc have invested to help companies such as Memphis

Meats and SuperMeat bring their products to market. Indian venture capital firms, angel investors, and industry must see the opportunity for growth and investment returns. This can be accomplished by hosting events, informational sessions, and demo days, and by inviting speakers from companies such as Memphis Meats, Perfect Day, etc.

4. **Regulatory landscape:**

As clean meat is a new technology, there needs to be a clear regulatory framework for safety and labeling. As in any country, the regulatory pathway for clean meat in India should be grounded in three principles (Specht, 2018):

- There should be one designated agency with primary oversight.As the end product of cellular agriculture is food, regulatory bodies that have been given the mandate of food safety have the most relevant expertise. In India, this body would be the Food Safety and Standards Authority of India (FSSAI), which is tasked with food safety.
- Secondly, clean meat producers should be informed about requirements for safety data and reporting, as well as review processes for different methods of production. Consumer safety evaluation and data in this arena will be mostly similar to conventional, animal-sourced meat. However, some elements, such as edible scaffolds (if used), may require a separate safety review process as determined by the regulators.
- Lastly, regulatory oversight should not be so complicated, as to disadvantage clean meat in the marketplace. Of course, safety and consumer confidence are of paramount importance, and the regulators should enable a quick path to market while adhering to these factors. The labeling conventions must also be adapted to allow clean meat to compete in the market.

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