Meat without the animals: cleaning our conscience with clean meat

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Abstract

In 2013 well-renowned Chef Richard McGeown cooked and presented live on air a hamburger made entirely from cultured stem cells. This was the culmination of several years of work in the lab of Dr Mark Post, a Dutch cardiologist turned food scientist. His work had constructed the burger with stem cells derived from cows that had been differentiated and grown in a laboratory. Since then the field of 'clean meat', as it is now known, has grown substantially. Many seriously consider it now as a viable option to sustain the world's population on both nutritional and environmental fronts. This progress has been made possible by scientists in academia as well as in start-ups funded by the likes of Richard Branson and Bill Gates. Although the technology is still at an early stage, increased resources and funding for clean meat research have led to several advances. Still, as the field moves forward, two main obstacles will need to be overcome: the perception of lab-grown meat by the public and governments, particularly regarding consumer uptake, regulation and legislation and secondly, the technical challenges that still remain. Among others, these challenges include the up-scaling of production to commercial levels and the engineering of more complex cellular structures to more closely replicate the taste, consistency and texture of meat.

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Introduction

In his 1932 essay Fifty Years Hence, Winston Churchill made the following prediction: "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." Despite being acknowledged 86 years ago, this absurdity still remains. There have been attempts to realise Churchill's vision using meat alternatives based on vegetable-derived products but, in the opinion of many, they fall short of accurately mimicking meat in all its sensations, from sight and feel to taste. Now, decades of biochemical research in tissue engineering, cell culture and protein science amongst other disciplines, are being brought together in the ground-breaking field of clean meat.

Clean meat is animal meat made by the process of culturing animal stem cells in such a way that they produce muscle tissue. It reproduces the 3D structure of animal fibres, closely replicating those found in conventional meat. The key difference between conventional and clean meat is that the latter is grown in a laboratory instead of inside a living organism which is then slaughtered. In the process of clean meat production, living animals are only used at the start to donate the initial stem cells (see Figure 1 for a detailed description).

In this piece, we describe the 'absurdity' that clean meat is tackling as well as how scientists and for-profit companies are achieving it. We outline the obstacles that the field of clean meat currently faces and give our views on its future directions, including the important issue of public acceptance on shifting food production from farms to laboratories.

The historical foundations and reasons for adopting clean meat

On the 5th of August 2013, Dr Mark Post of the University of Maastricht in the Netherlands unveiled the first burger grown in a lab, thus being the first made of clean meat. This was no small feat: the technologies necessary to grow such a piece of animal tissue were made possible by the preceding 15 years of stem cell and tissue research. This had not been conducted for the purpose of growing muscle for human consumption but primarily in the field of regenerative medicine. However, Dr Post, formerly an assistant professor of Medicine at Harvard Medical School, realised that this research could be used to develop a new avenue of food technology and he pivoted into the fields of vascular physiology and tissue engineering, moving to the Netherlands to establish research groups in these areas.

That world-first clean meat burger from his research group cost over $300,000 to produce and was funded in part by Google-cofounder Sergey Brin. Since those early days when the goal was a proof-of-concept example of meat grown in the lab that was fit for human consumption, the cost of clean meat has gone down to $5,280/kg (as of June 2017) [1].

The successful production of clean meat could, in theory, solve some of the biggest problems that face humanity. One of those problems is that if the global demand for meat increases due to developing world economies becoming wealthier, the current methods of food production will not be able to meet this growing demand [2,3]. Some estimates even put forward that livestock meat production is already at its upper limit [3]. Combined with growing populations, the limited production capacity could set up the conditions necessary for a drastic global shortage of meat. Arguably, meat is already on track to become a luxury commodity affordable to a wealthy minority [4]. Clean meat may be able to tackle this looming problem as it can theoretically be produced more cost-effectively than farmed meat.

A second problem that wide-scale clean meat production could solve is that there are well-established environmental burdens associated with the agricultural livestock industry. Around 40% of total CO_2 emissions are attributed to this industry, and factory farming also consumes considerable land, energy and water [2]. Energy usage estimates have recently been made for clean meat production: making 1000 kg of cultured meat would require 26 to 33 GJ energy. This figure is between 7 to 45% lower than the conventional livestock energy consumption [5]. The study also estimates that clean production will use 99% less land and reduce water consumption by 82 to 96% [5].

Furthermore, there are considerable problems regarding the ethics of factory farming animals, which is the large-scale industrial process that produces the vast majority of the meat consumed world-wide. The issue of animal welfare divides the public opinion however, since fierce proponents on either side of the animal rights debate are often unwilling to make comprises or come to agreements. For instance, animal rights campaigners are perceived as extremists, and potentially do more harm than good when they use aggressive campaign slogans and scare tactics.

Still there are good arguments that raising and slaughtering approximately 70 billion land animals every year—most of them 'broiler chickens' raised specifically for meat production rather than for eggs—could likely be a pressing moral concern. Modern day scholars like Peter Singer have long argued the moral importance of animal sentience, and Yuval Noah Harari has even described industrial factory farming as 'perhaps the worst crime in history' [6]. Recently, detractors of animal factory farming have used educational documentaries to cause viewers to acknowledge the detachment that exists between a meat consumer and the meat producer (this detachment is strongest in the Western world, where the food is usually bought pre-packed in supermarkets.) Films such as *Cowspiracy* give an insight into the world of factory farming and show viewers the harsh methods that allow the mass production of meat to supply the current demand.

Finally, there are also consequences to human welfare that arise from modern day factory farming. The greatest concerns are the use of growth-promoting hormones and the gross overuse of antibiotics. Eighty percent of antibiotics used in the USA are given to livestock [7] and the inevitable development and proliferation of antibiotic resistance is rapidly manifesting as a global catastrophe. Furthermore, the incredibly densely populated spaces within factory farms are a major repository of potential human pathogens. Given that an estimated 60% of all human infectious pathogens are zoonotic in nature, this dense population represents an unimaginable public health concern [8]. In this respect, clean meat offers an alternative because the conditions of a laboratory-based facility will be fully sterilised and there will be no need for antibiotic use. Moreover, few contagious pathogens that pose a public health threat infect tissue or muscle cells themselves, so in theory the pool of cells used for clean meat will have a reduced capacity as a repository for potential human disease-causing agents.

Clean meat in 2018 - what, how and who?

The ability to produce clean meat is seen by many as a necessary development for there to be sustainable food production in the future. By being able to grow meat in a lab, the issues mentioned above can be addressed without altering current eating habits, as the overriding aim of the clean meat field is to produce meat without being more expensive than conventional meat.

Although tissue engineering techniques have only just become advanced enough to be used to grow animal tissue in laboratories for food, various meat alternatives have already been produced. The science behind these does not require the production of animal tissue from cells but the use of non-meat-based analogues to replicate the texture and taste of meat. Hence, whilst acellular production of meat substitutes relies on trying to mimic meat's flavour and texture with alternative products, clean meat production aims to grow the actual cells that make up muscle tissue.

Acellular meat alternatives

Today, acellular-based meat substitutes are ubiquitous in supermarkets in the UK and US. The brand *Quorn* has been available for over three decades (it launched in 1985). Most products are based on soy (e.g. Tofu), wheat proteins (*Seitan*) or mycoprotein (*Quorn*) as these sources comprise high quantities of protein, enabling them to resemble meat's texture. However, despite continuing improvements in technology, these products are not able to fully mimic meat in terms of texture or taste. With this in mind, Stanford professor Patrick O'Brown launched Impossible Foods in 2011 to develop better meat substitutes and combat industrial animal agriculture. After 5 years of development, the company launched the *Impossible Burger* which they claim to use 95% less land, 74% less water, and emit approximately 87% less greenhouse gas than a burger made from cow meat [9]. Importantly, this burger resembles meat more closely than any of its predecessors due to the intensive research put into creating the composition. A chemical called leghaemoglobin, extracted from soybeans, causes the burger to leak a red substance that resembles bleeding. The discovery of this compound, and the ability to mass produce it in genetically modified yeast was the greatest leap forward in developing a more accurate meat analogue. Yeast can be engineered to produce leghaemoglobin more efficiently than soybeans . Further research into how to mimic the taste, texture and appearance of meat led to the development of a blend of vegetable fats and proteins that are used inside the *Impossible Burger*. Potato protein for example makes the burger softer whilst coconut fat causes it to sizzle when cooked. With the production of their *Impossible Burger*, Impossible Foods has demonstrated how biochemical research can be used to develop a huge step forward in meat alternatives.

Cellular techniques to make clean meat

Many still believe that the production of meat substitutes must be done with animal tissue so as to move away from the minced-meat alternatives that are the only ones available so far, and to develop more accurate meat mimics. This would offer enhancements in appearance, smell, texture and taste over conventional meat alternatives.

Clean meat exploits animal cells, obtained with biopsies, to grow animal tissues in the laboratory in a controlled fashion. Because the tissue would be made from animal cells, it would theoretically be identical to meat from slaughtered animals. The work of Dr Mark Post is an example of these so called cellular methods, but there are now around 18 start-ups using similar techniques [11].

As shown in the process flowchart in Figure 1, cellular methods generally begin with a minimally invasive muscle biopsy [10] to extract myosatellite stem cells from the animal (the cells that build and repair muscle tissue in healthy animals [12]). The stem cells are then grown in culture inside a laboratory using well-developed techniques that are already widely used in research. Once there a sufficient number of these stem cells in the culture, certain conditions and chemicals are used to make them differentiate into cells that produce muscle fibres – known as myoblast cells. Correct synthesis of muscle fibres is a crucial step for tissue production in living organisms, and a variety of external cues are required for this, including the presence of growth factors and mechanical stimulation. Successful clean meat production must therefore replicate these processes. To achieve this, electric impulses are applied whilst the cells develop as fibres. Growth nutrients are provided in the form of foetal bovine serum. Further research is undergoing to identify additional components needed for muscle tissue production such as fat-providing cells (adipocytes) [13]. In order to produce different forms of meat (e.g. steaks rather than burgers) a synthetic skeleton called a scaffold is provided for the fibres to grow on. The scaffold gives shape to the clean meat, and also provides routes for nutrient entry into the centre of the tissue structure.

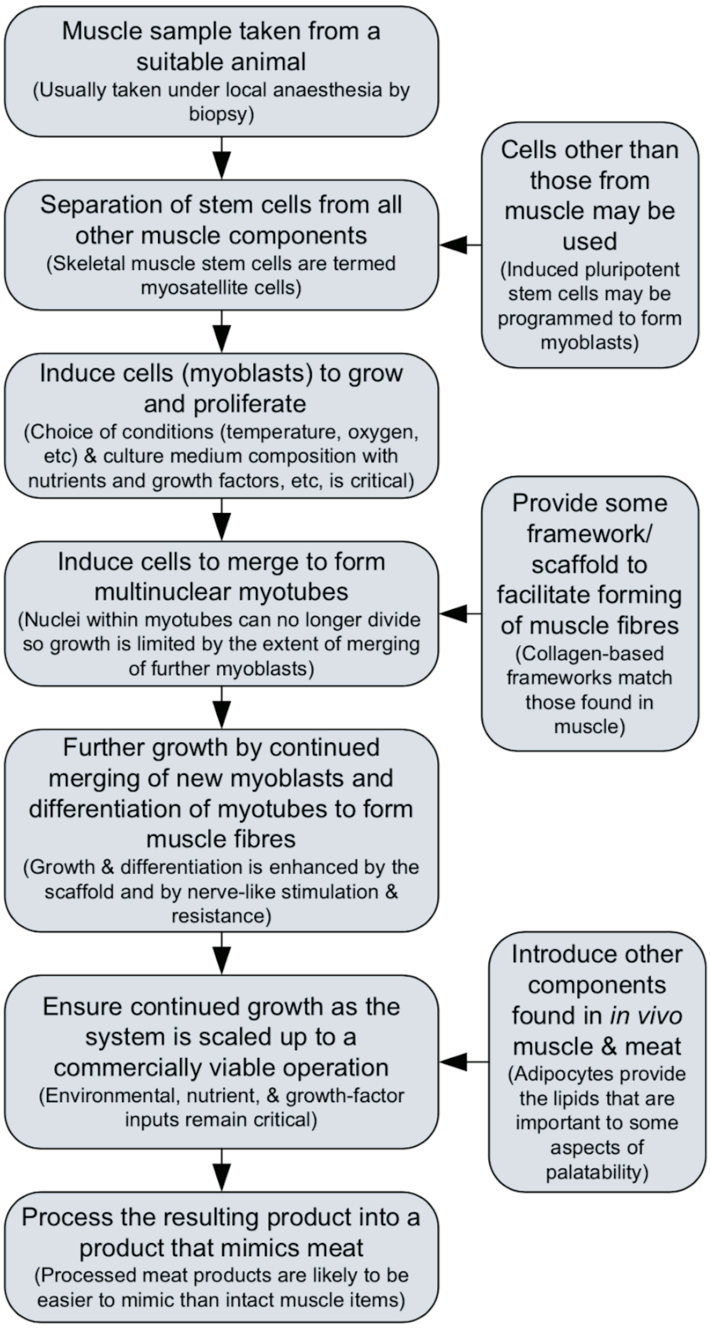

Figure 1: A flowchart to show the main steps required in the production of a clean meat product

Two huge advantages of clean meat can be made obvious. Firstly, the ability to grow cells in sterile culture conditions allows for a huge reduction in the amount of antibiotics used in food production as previously mentioned. Secondly, the control over which chemicals and nutrients are added to the cell culture permits alteration in the fats, proteins and other biomolecules produced by the cells. This creates the potential for cultured meat to be more nutritional than traditional meat as it could be possible, for example, to decrease the content of cholesterol and increase the protein content.

The current commercial climate of clean meat research

The scientific developments and breakthroughs currently being made in the clean meat field are primarily in the laboratories of start-ups developed and funded through incubators, investment funds and private investors. Impossible Foods, for example, has raised over $180 million in funding from sources including Google Ventures and Bill Gates [14]. The latter has also invested in Memphis Meats, a clean meat company that relies on cellular systems and which expects to release products onto the market in 2021. Other clean meat companies are still in early development stages and have only demonstrated products at publicity events. Impossible Foods, on the other hand, has already released products throughout America, from chain stores to Michelin Star restaurants [14]. While there are many obstacles which still need to be overcome by cellular based techniques for clean meat production, at least there has been a precedent set for consumer adoption of acellular meat substitutes like the *Impossible Burger*. We will later discuss these obstacles in more detail.

Traditionally, incubators have focussed on technology start-ups but they are now transitioning to ventures founded on deep science. An example is IndieBio, a US-based incubator that is tailored to the biological sciences and to scientists that want to commercialise their research. They provide funding of $250,000 as well as laboratory space to help scientists create viable products from their initial research in the space of four months. Finless Foods is the most prominent clean meat company to have gone through the IndieBio accelerator; as their name suggests, they are attempting to produce lab-grown fish meat using stem cells derived from fish tissue [15]. Their aim is to bypass current fish farming methods to make clean fish meat that is healthier, cheaper, more environmentally friendly and produced with more sustainable methods.

Alongside this, scientific research into clean meat in the for-profit world is also supported in academia. The Oxford Martin School is currently working to tackle global problems using interdisciplinary research. As it is stated on its website, the school acknowledges food production and sustainability as a great global challenge of this century: "Without radical change to the way we produce and consume food […] there is a substantial risk of significant increases in food prices with major political, environmental and humanitarian consequences." [16]. Its specific interdisciplinary food research programme brings together the private sector, academia and government to solve the global food crisis. One of the aspects of the programme includes the development of clean meat production. This interdisciplinary approach is extremely important because the obstacles which face clean meat production are not purely scientific, as the next section shows.

Obstacles to the production and adoption of clean meat

There are three main technological considerations that are presently withholding the large-scale production of clean meat: the type of cell line used for maximal meat production efficiency and for different types of meat, improvements in cell culture media used to grow cells and finally the scaffold that is used for the fibres to assemble on [17].

Cell lines (for example, the myosatelleite stem cells), must firstly be derived from an appropriate animal species because the replacement of current farming methods will require successful production of replacements for all types of meat e.g. clean chicken, clean lamb etc. Cell lines must also have stable genetics for consistent long-term production of clean meat. Finally, they must be optimised for large scale culture as cells usually behave differently when grown in industrial scales.

The culture medium in which the cells are grown will need to be rapidly produced on a large scale and at low costs. It will also need to have an optimal combination of synthetic growth factors to support cell growth and, importantly, it should not contain products derived from animals (as is the current gold-standard media component foetal bovine serum). This last constraint is required to make clean meat truly clean since the production of foetal bovine serum requires animal slaughter. As was mentioned earlier, the main aim of the clean meat field is to ensure global meat demand can be met without the rearing and slaughter of animals. As decades of cell culture in research has required foetal bovine serum, its replacement will need a huge paradigm shift and so this particular aspect of clean meat production represents a particularly challenging obstacle for the clean meat industry.

Another massive hurdle is the development of the scaffolds that the cells are grown on because they must allow cell adhesion to their surface and also support the growth of blood vessels whilst being fit for human consumption. Moreover, different scaffolds will be needed for different types of clean meat because the 3D shapes, nutrient requirements and number of blood vessels varies significantly between different tissues. As an example, a fish fillet and steak are constituted from tremendously different types of tissue as the former is white meat with little fat and no blood vessels whilst the latter has a high amount of blood vessels as well as a high protein and fat content. This would need scaffolds that would allow physical stimulation of the muscle fibres as they produce tissue. In order for the development of suitable scaffold, extensive scientific collaboration has already been required and will need to continue. For all the requirements above to be met, the skills of material scientists need to be combined with those of biochemists and tissue scientists.

There are also considerable non-scientific obstacles before clean meat can become a viable consumer product. It is currently unclear which organisations would actually regulate clean meat production. In the United States, the safety and quality of conventional livestock meat is under the jurisdiction of the US Department of Agriculture (USDA), whereas cell cultures and biomedicine are regulated by the Food and Drug Agency (FDA) [18].

Another obstacle may be the divisions within the industry about what clean meat should actually be. Some of the most influential names in the industry, including Bruce Friedrich of The Good Food Institute, think that it would be bad to deviate from the normal composition of meat and change its fat and protein content, as this may be preferable from a consumer standpoint. However, others such as the CEO of Memphis Meats, Uma Valeti, think that a precision-engineered product will enhance consumer uptake—for example low fat versions of clean meat for health conscious buyers. Although both versions of livestock meat currently exist, it is unclear which marketing tactic will be optimal for the adoption of clean meat.

Following from this, a market for clean meat must be created so that the scientific and technological investment is not in vain. Scientists insist that the product is biologically identical to meat grown on animals, but the consumer opinion does not seem to agree (as attested by several polls). A 2016 survey carried out in America revealed that most of the participants were willing to try clean meat but only one third of the total was 'definitely or probably willing' to eat clean meat regularly in place of farmed meat [19]. The survey notes that the positive attitudes towards clean meat arise from the potential environmental and public health benefits of product, while negative attitudes come from reservations about the feasibility of industrial scaling and overtones of the 'unnaturalness' of meat grown in the laboratory (although this last query is incorrect because clean meat will be grown in bioreactors). This disgust factor may be the biggest hurdle that proponents of clean meat may face, perhaps even more so than the technological barriers.

Summary and our proposals for the future of clean meat

In summary, we believe that the current state of clean meat research looks set to overcome some of the world's greatest problems. These include the uncertainty of supplying meat to the world's growing wealthy population; the ethical considerations regarding the suffering of animals on factory farms; and the potential danger to human populations from factory farming practices such as zoonotic pathogen escape and emerging antibiotic resistance. We discussed the technological hurdles of upscaling cellular growth, efficient growth in serum free media and the availability of edible scaffolds. Non-technical challenges like the public perception of clean meat may prove to be the biggest barriers.

In light of the current state of the field of clean meat field and its main obstacles, we consider that there are four key areas where there is room for improvement: there is a need of better scientific collaboration; alternatives to foetal bovine serum for media should be produce; public engagement with clean meat research should be increased; a policy infrastructure governing the sale, distribution and regulation of clean meat for the relevant authorities should be brainstormed. We believe the first of these is important as developing clean meat requires work from a wide range of scientific disciplines such as tissue engineering, materials science and stem cell research. Following on from this, the development of non-animal derived culture media will also be necessary for clean meat to be truly free of animal slaughter, without which clean meat will achieve the goal of replacing livestock animals from the human diet. This is in development already but will require further interdisciplinary research to determine the specific molecules a growth medium requires and mass produce them in commercial quantities.

Finally, increased public and authority engagement is a necessity to educate the public on the problems of current meat production techniques as well as ensuring the proper publicity and regulation of clean meat production. Without this there may be a chance that a sizeable market for clean meat will not exist at the right time and the project discontinued, when in other circumstances there might have already been a willing consumer base—nurtured through careful marketing and tactful public education about the failures of factory farming and the viability of clean meat. Appropriate development of the clean meat industry also relies on the imposition of regulatory bodies and distribution networks poised to turn the product into a widely available commodity.

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