La carne cultivada: ¿mito o realidad?

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1. What is Cultivated Meat?
2. How is Cultivated Meat made?
3. What are the benefits of Cultivated Meat?
4. What are the differences from conventional meat?
5. What about social issues?
6. When will Cultivated Meat make it to market?

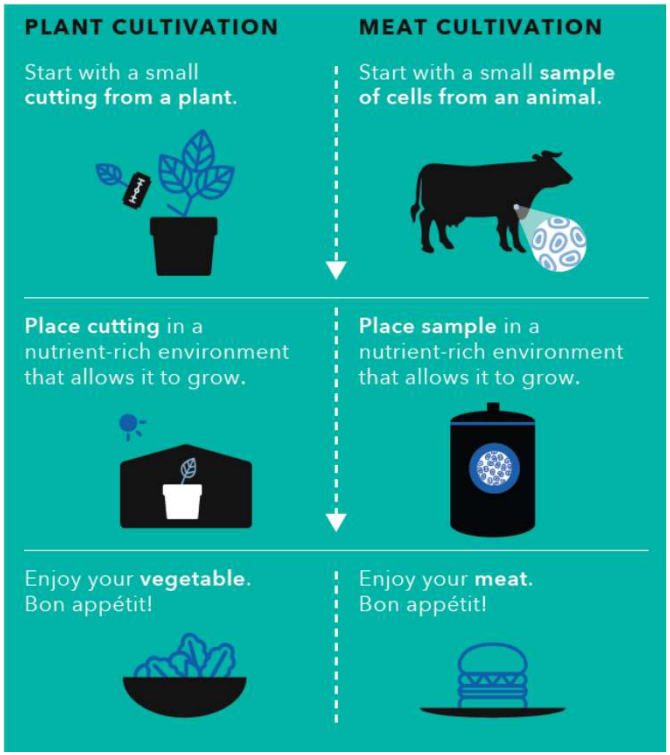
1. What is Cultivated Meat?

Words matter!

…lab-grown meat, cell meat
"in vitro" meat, synthetic meat
artificial meat, clean meat, …

CULTIVATED MEAT - CULTURED MEAT

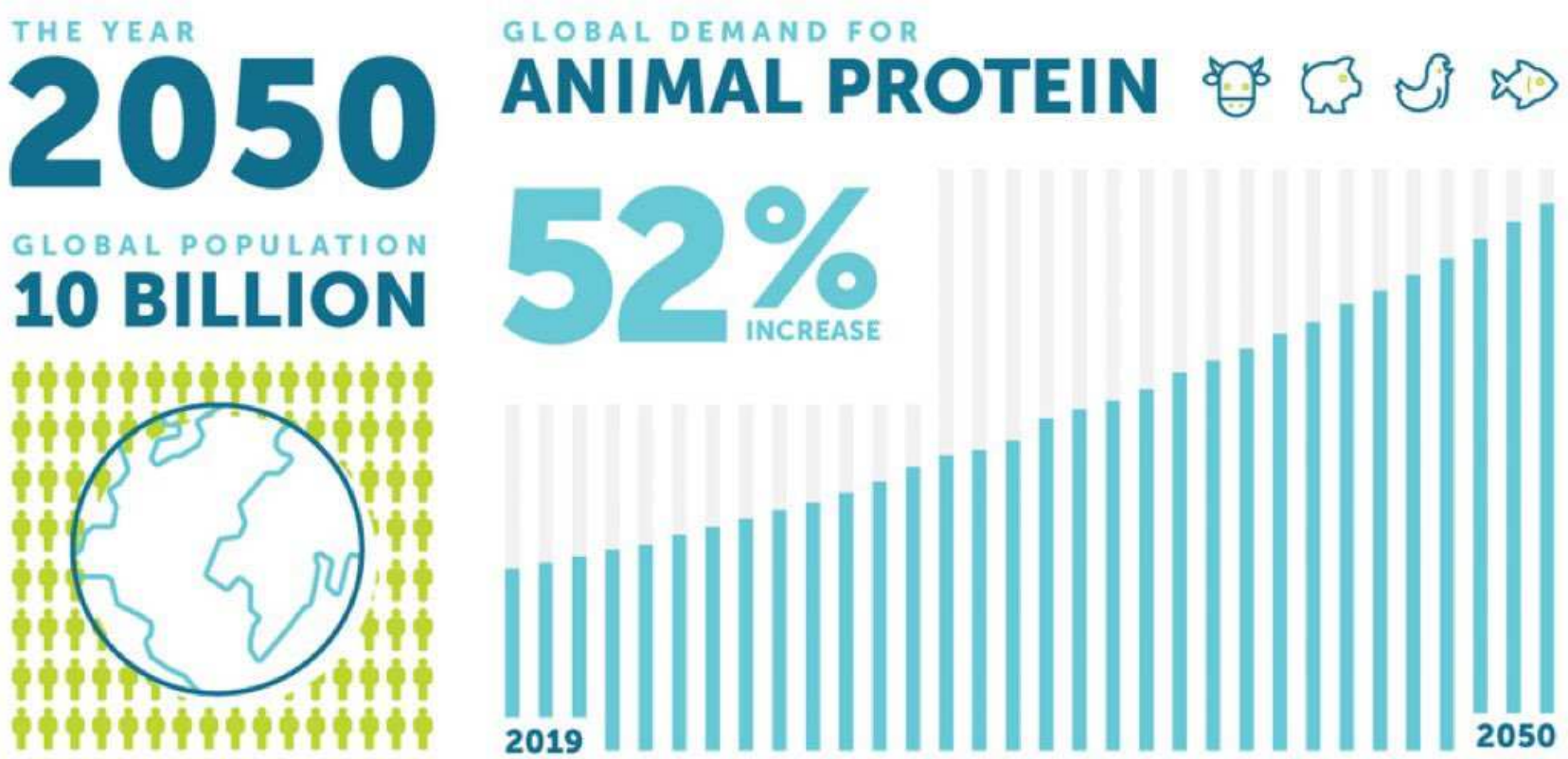
- ✓ **Is an animal tissue which does not proceed directly from the body of an animal**
- ✓ **Is produced from an "*in vitro*" cultivation of cells previously extracted from animals**
- ✓ **Is identical to conventional meat at cellular level**



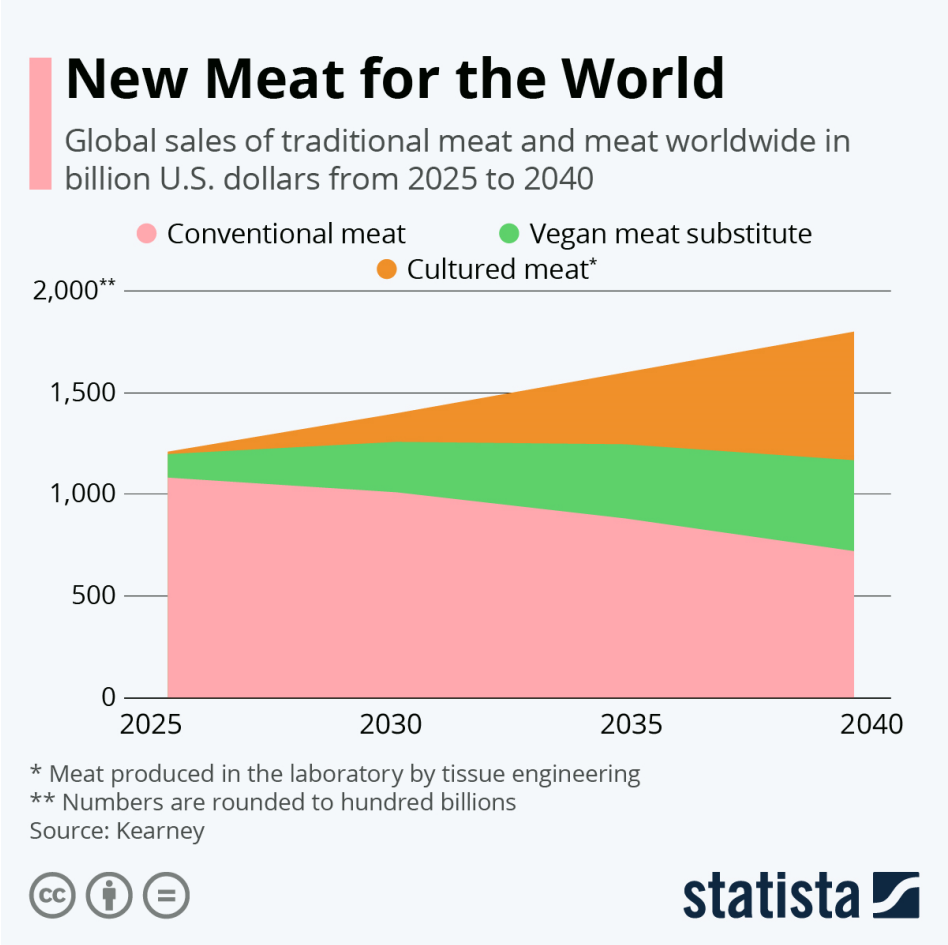
https://gfi.org/blog/cultivatedmeat/

Cultivated meat should not be confused with meat analogues or “vegetal meats”, which are vegetarian products fabricated with vegetal proteins

The "*Protein Gap*"



The meat market



https://www.statista.com/chart/20464/global-meat-consumption/

"With a greater knowledge of what are called hormones, i.e. the chemical messengers in our blood, it will be possible to control growth.
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."

Winston Churchill, "*Strand Magazine*" 1931

Timeline of cultivated meat

1971 – Muscular fibers cultivated “in vitro”

1995 – FDA approves “in vitro” meat techniques for NASA

2002 – NASA/NSR/Touro Applied BioScience Research Consortium produce “in vitro” Goldfish edible muscle

2013 – Mark Post (Maastricht University) presented 1st cultured hamburger

https://www.maastrichtuniversity.nl/news/what%E2%80%99s-been-going-%E2%80%98hamburger-professor%E2%80%99

December 2020

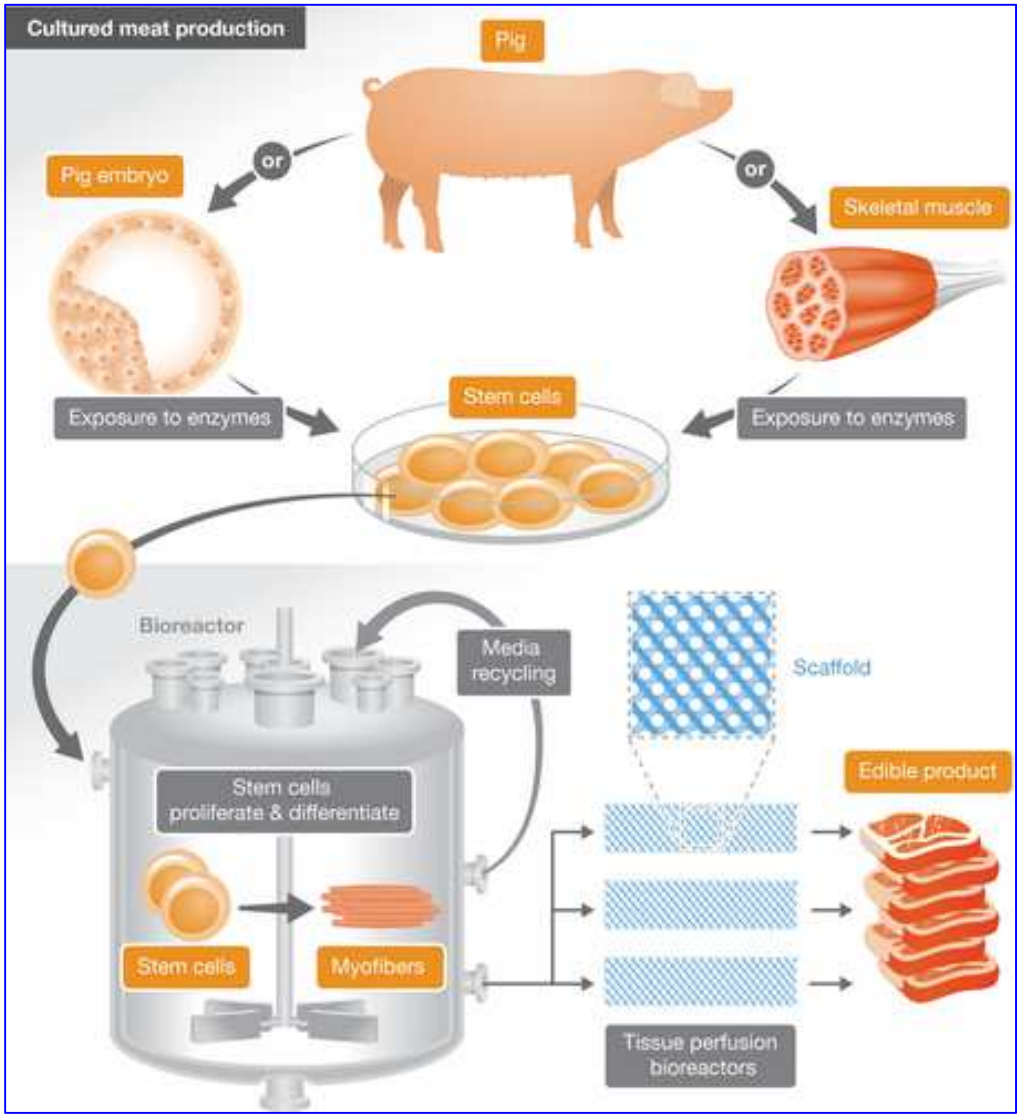
Singapore gives regulatory approval for the world's first "cultivated chicken meat" that does not come from slaughtered animals (start-up Good Meat)

Good Meat chicken Nuggets https://www.ju.st/

2. How is Cultivated Meat made?

The process in a nutshell

The process for producing cultivated meat is achieved by applying technologies and biomaterials already developed for tissue engineering



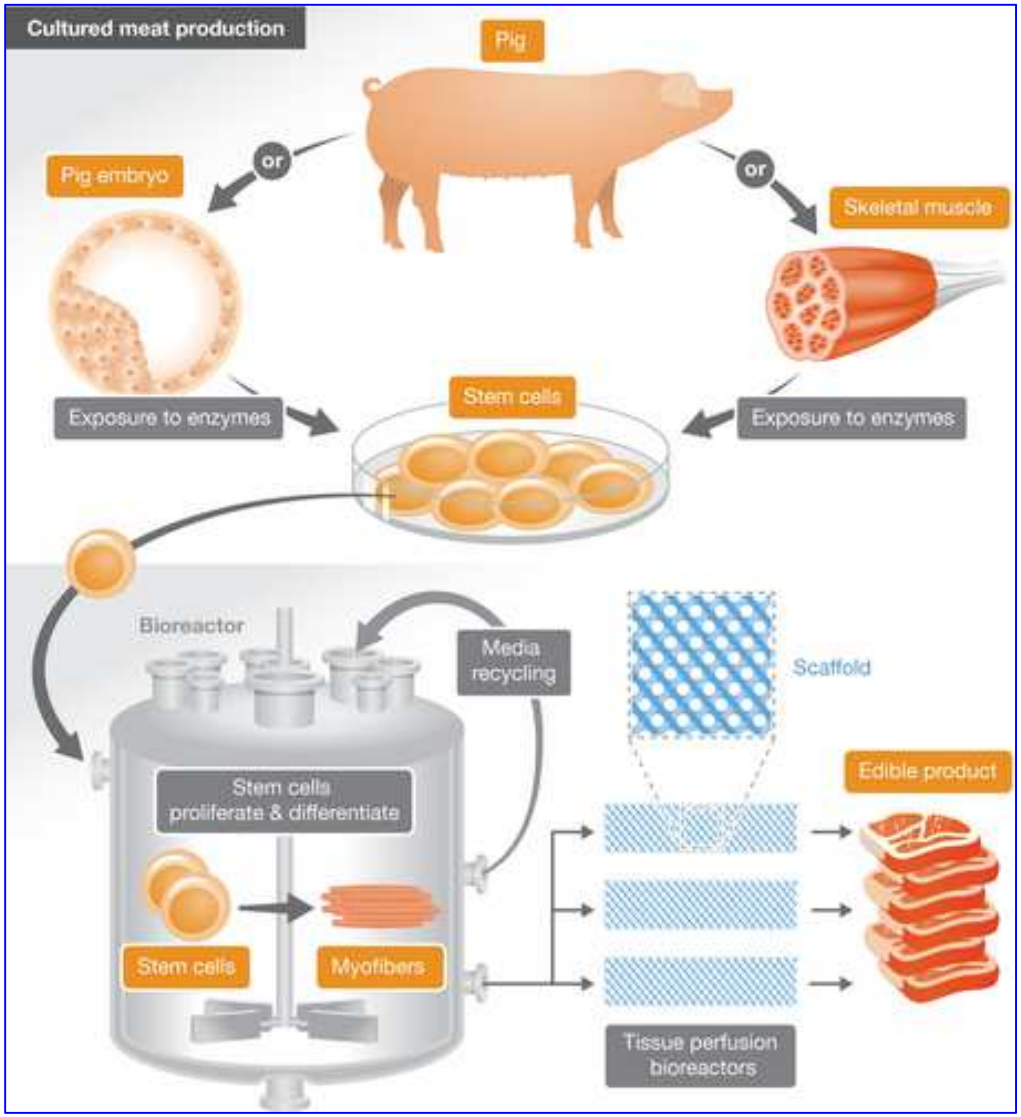
Hanna Tuomisto https://doi.org/10.15252/embr.201847395

The process in a nutshell

Production involves **2 main steps:**

-a **biopsy** to isolate stem cells from an animal

-the **proliferation** and **differentiation** of these isolated stem cells into desired tissues (e.g. skeletal muscles) in a suitable cell culture medium



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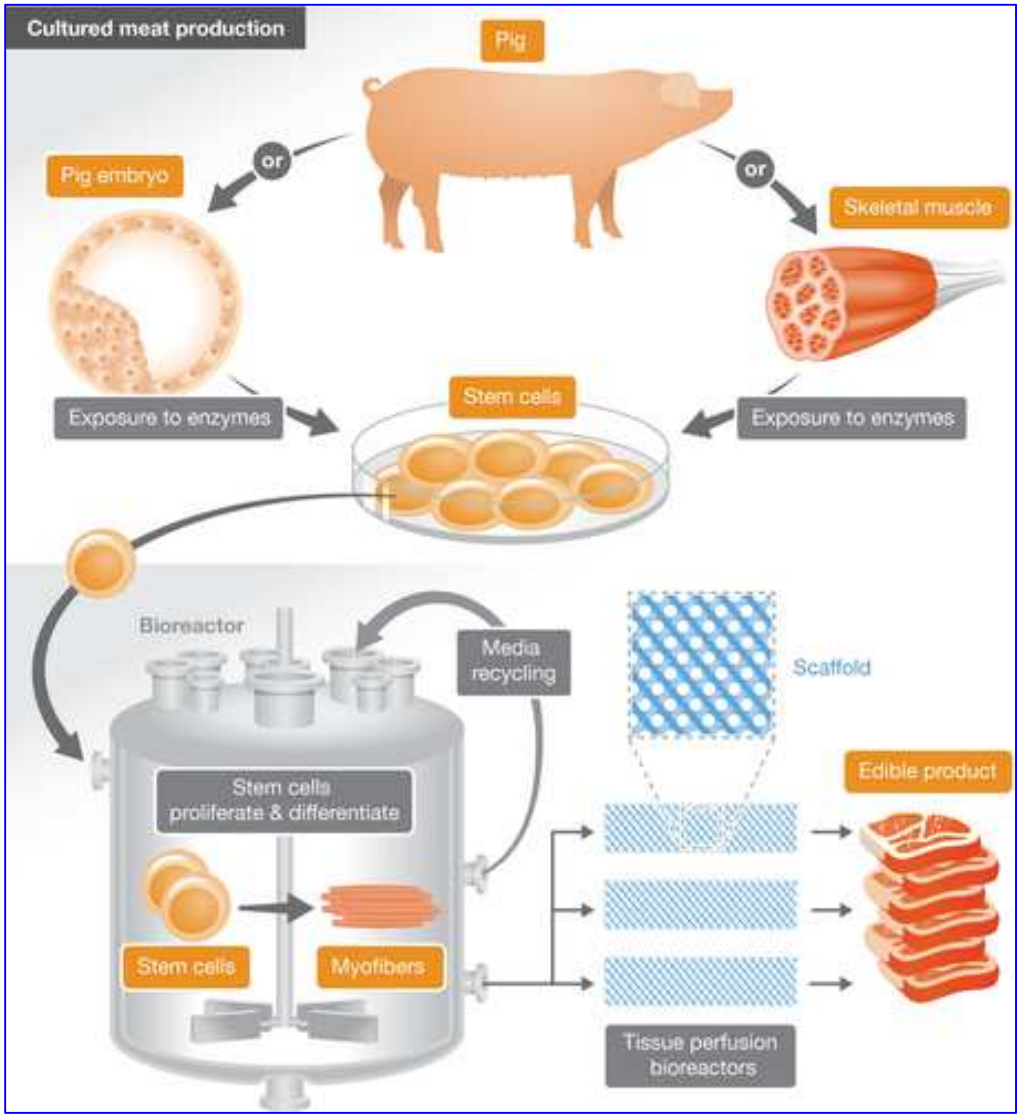
The process in a nutshell

In the process, the growing cells can be attached to **scaffolding materials**, such as collagen-like gel polymers, working as a support network for the tissue development



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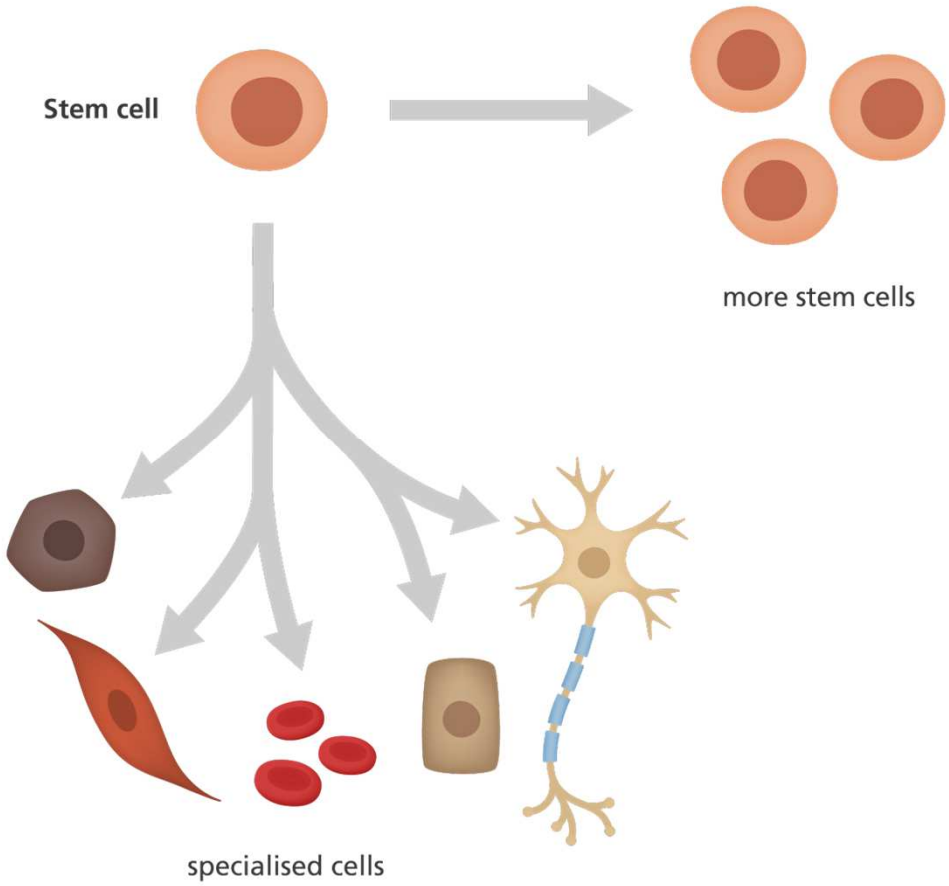
Stem Cells

Stem cells have two unique properties that enable them to :

-divide over and over again to produce new cells

-change into the other types of cell



https://www.yourgenome.org/facts/what-is-a-stem-cell

Cell selection

The suitability of the starting cells is based on their:

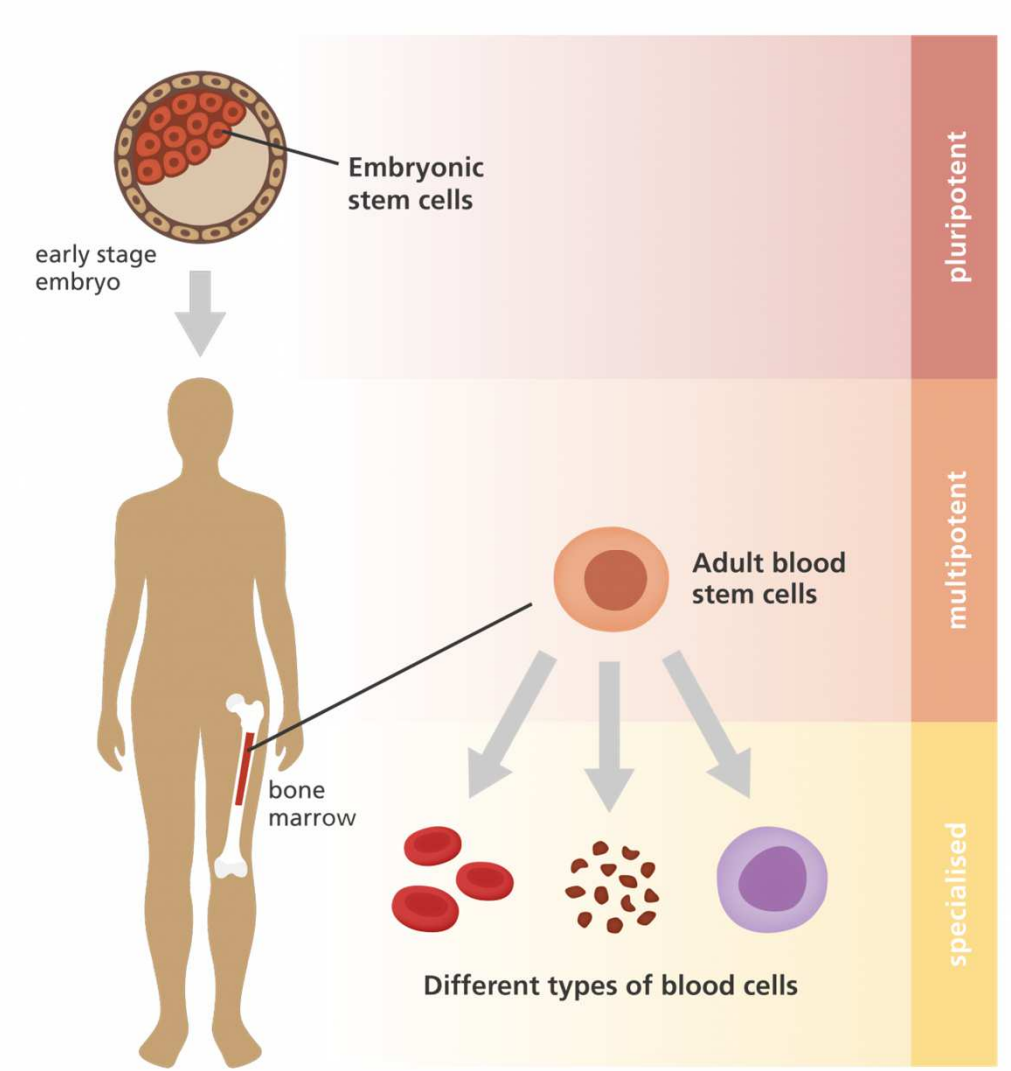
-ability to replicate and proliferate while retaining their potential to differentiate in one or more tissue lineages (self-renewal)

-capacity to expand and differentiate into skeletal muscle, the predominant constituent of most meats.

Different types of stem cell

Embryonic Stem Cells (ESCs) supply new cells for an embryo as it grows and develops into a baby.

These stem cells are said to be **pluripotent**, which means they can change into any cell in the body.



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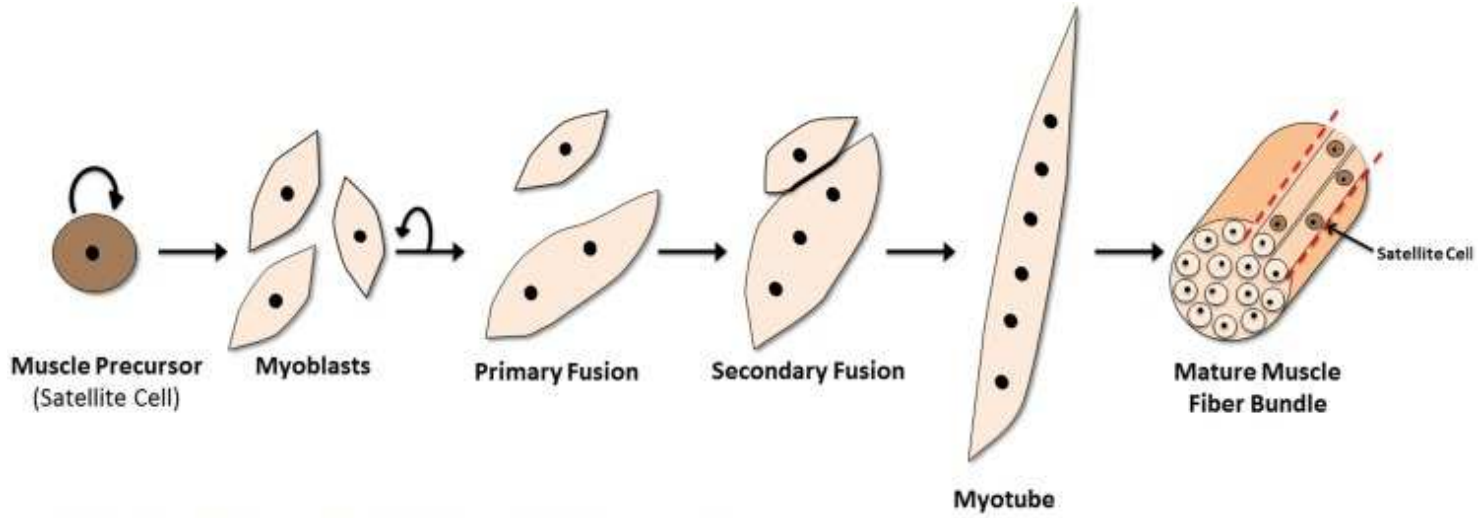
Different types of stem cell



Muscle Stem Cells (**MSCs**) are **multipotent** (they can only change into some cells in the body, not any cell) cells found in mature muscle. Under normal conditions, MSCs are quiescent but could give rise to satellite cells or differentiated skeletal muscle cells.

MSCs were used to create the first cultured meat hamburger prototype.

Different types of stem cell

Induced pluripotent stem cells (IPSC)

are stem cells that scientists make in the laboratory by taking normal adult cells, like skin or blood cells, and reprogramming them to become stem cells.

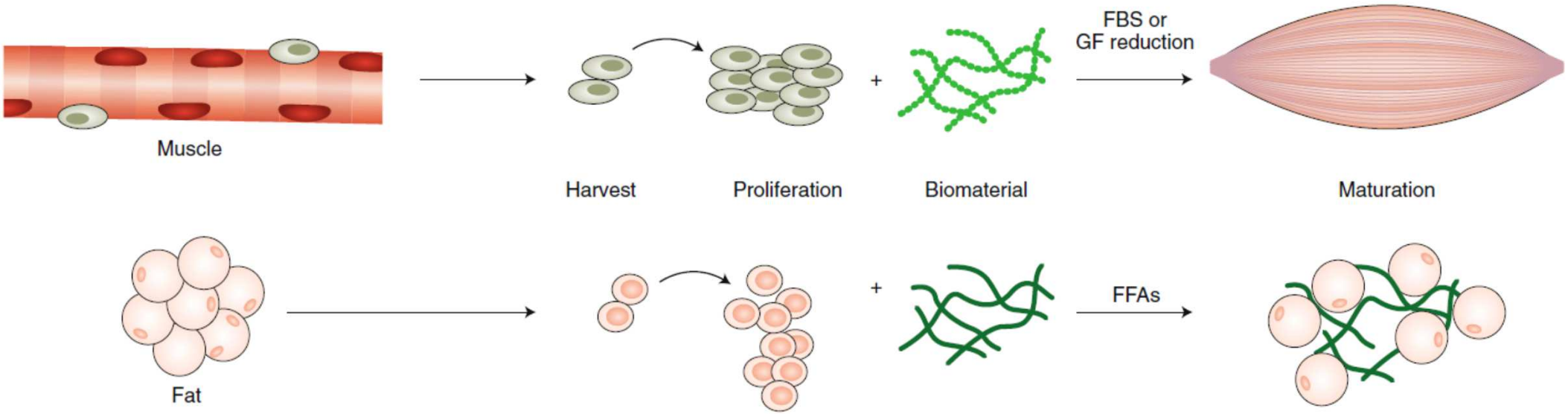
Just like embryonic stem cells, they are **pluripotent** and have an **indefinite renewal capacity**

Ethical issues on the use of embryonic stems cells may be circumvented.

https://www.yourgenome.org/facts/what-is-a-stem-cell

Stem cells are:
-harvested by a biopsy from a living animal
-expanded in vitro to generate a large number of cells
-differentiated to mature muscle fibres and pieces of adipose tissue in presence of scaffold biomaterials

During maturation cells are also stimulated electrically or mechanically to make easier their development.



Post et al., 2020 https://doi.org/10.1038/s43016-020-0112-z

Cell culture medium

Cell growth need media contain:

-**nutrients** (glucose and amino acids)

-**fetal bovine serum (FBS)** or equivalent serum-free differentiation which provide essential nutrients, including hormonal and differentiation factors for cell proliferation (growth hormone and insulin), transport proteins (transferrin and transcortin) and growth factors (epithelial, endothelial, fibroblast and insulin-like growth factors) which regulate cellular activities, including stimulation of proliferation and differentiation, by activating signaling pathways

However, there remains a **lack of knowledge** around muscle-specific signaling pathways and safety for use in food production, and the optimal dosage data for in-vitro myocyte cultivation still needs to be established.

Post et al., 2020 https://doi.org/10.1038/s43016-020-0112-z

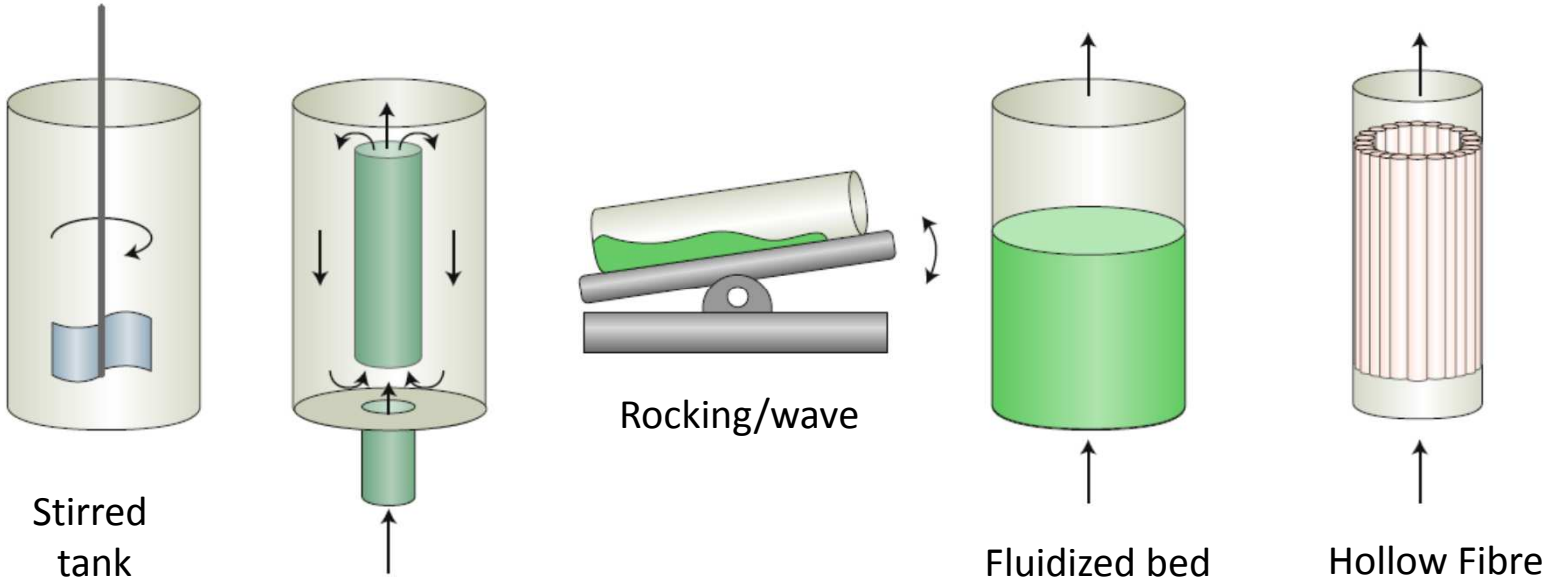
Cell culture medium

Cell culture medium is **one of the major cost** for the upscaling of stem cell production.
Animal-derived components, including fetal bovine serum (FBS), are environmentally unsustainable, introduce contamination risks with undefined substances and violate the ethical principle of using fewer animals.
Alternative serum-free media have been suggested depending on cell type:

- ✓ (*e.g.*, Ultroser™ G, B27 TM)
- ✓ yeast extracts
- ✓ hydrolysates from food by-products, chicken carcass, cod backbone, pork plasma, eggshell membrane, egg white powder,
- ✓ algal extracts

By adding myoglobin and heme proteins to cultures of bovine muscle cells could assist in modifying the color of cultivated beef to more closely resemble that of conventional beef.

Bioreactors

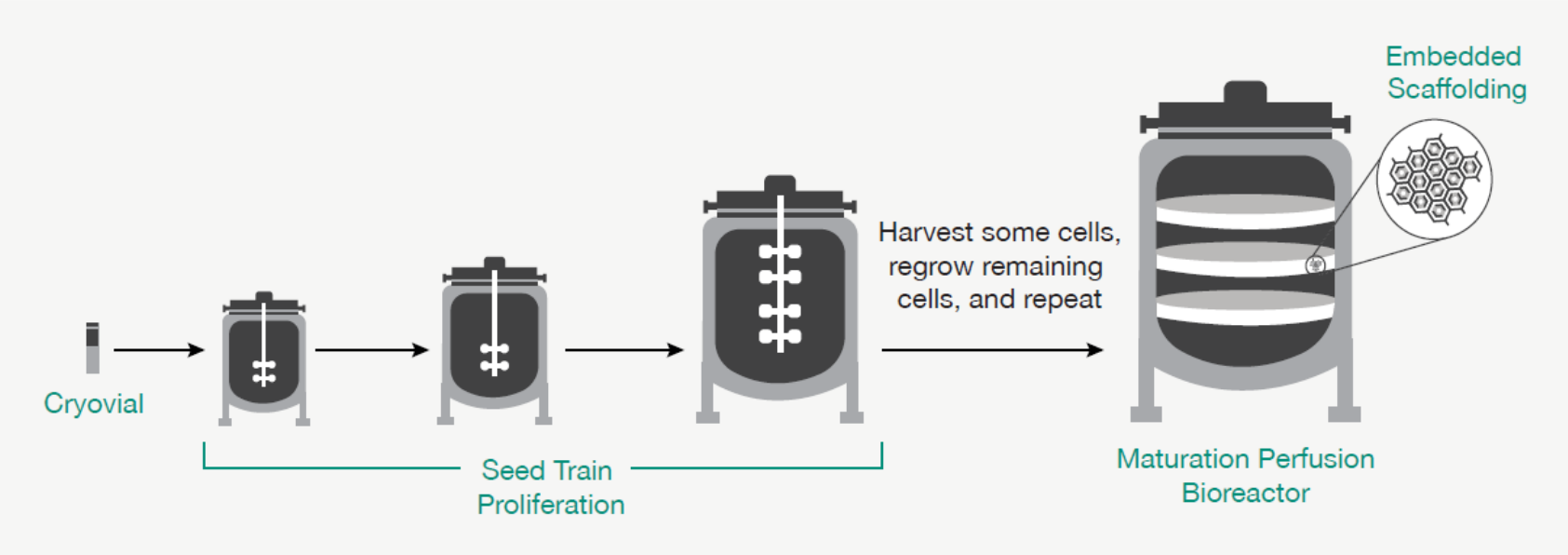


Source: Post et al., 2020 https://doi.org/10.1038/s43016-020-0112-z

The ultimate goal of bioreactor development is to increase the percentage of nutrients in the medium that is converted to edible animal tissue, known as the medium conversion ratio, equivalent to the feed conversion in traditional livestock meat production. Low growth rate, metabolic inefficiency, catabolite (CO_2, NH_3), in shear-inhibition, and induced cell damage will all limit practical bioreactor volume and attainable cell density.

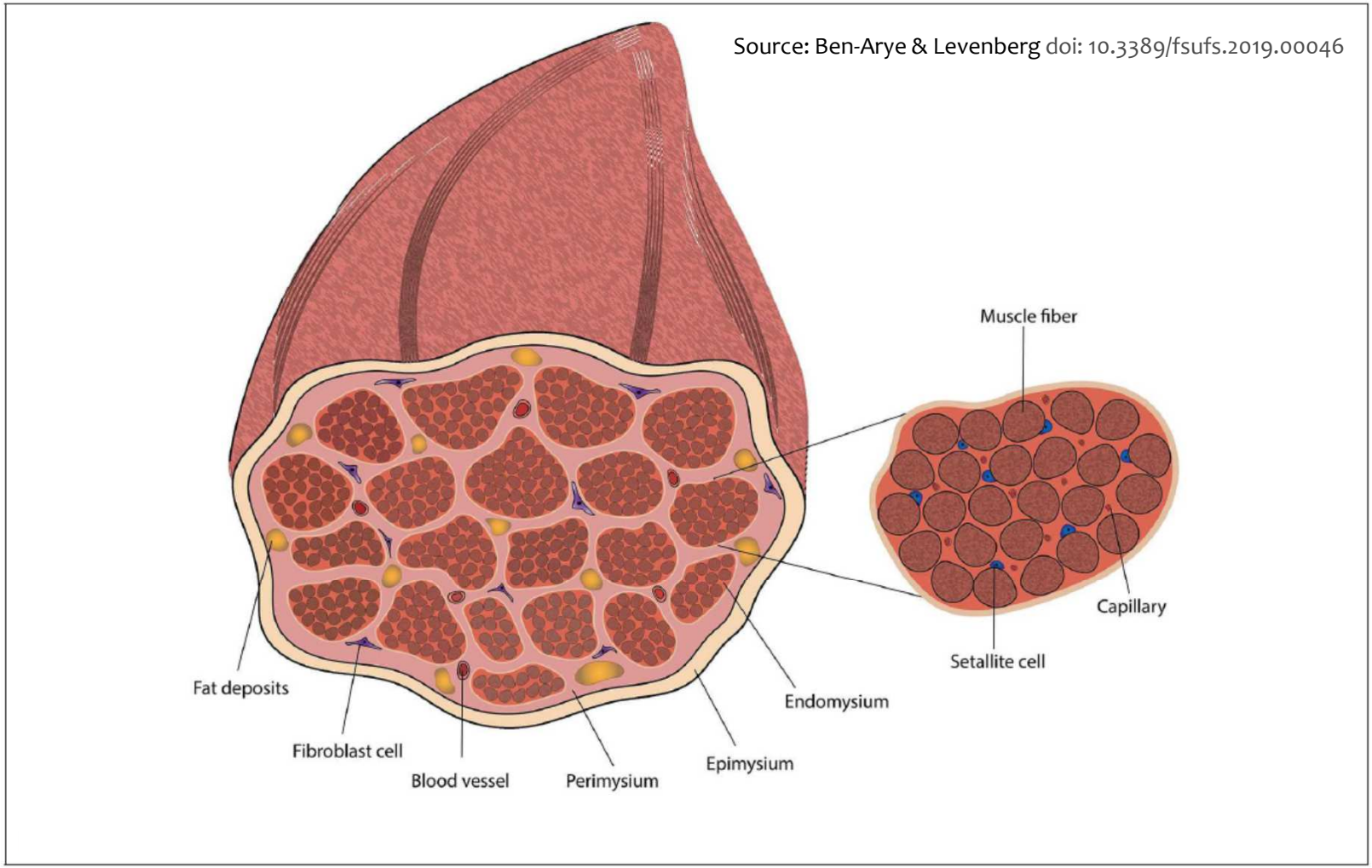
Bioreactors

- ✓ Equipment and facilities must have adequate **microbial contamination safeguards**
- ✓ Cultures can be used continuously for some number of generations, but periodically they are restarted from frozen stocks **to avoid genetic drift**
- ✓ A **29-day cycle** is sufficient to scale a frozen vial of 10^6 cells to **two tons of cell mass** in a 20,000 L tank



Source: Swartz, 2019. https://gfi.org/wp-content/uploads/2021/01/Cell-Based_Meat_CEP_Oct2019.pdf

Diagram of skeletal muscle tissue



….a real meat experience?

Most cultured meats consist solely of muscle tissue

Minced cultured meat composed of muscle and fat are made by separately culturing different cells (muscle fibres and adipose organoids), which are later combined to form the final cultured meat product.

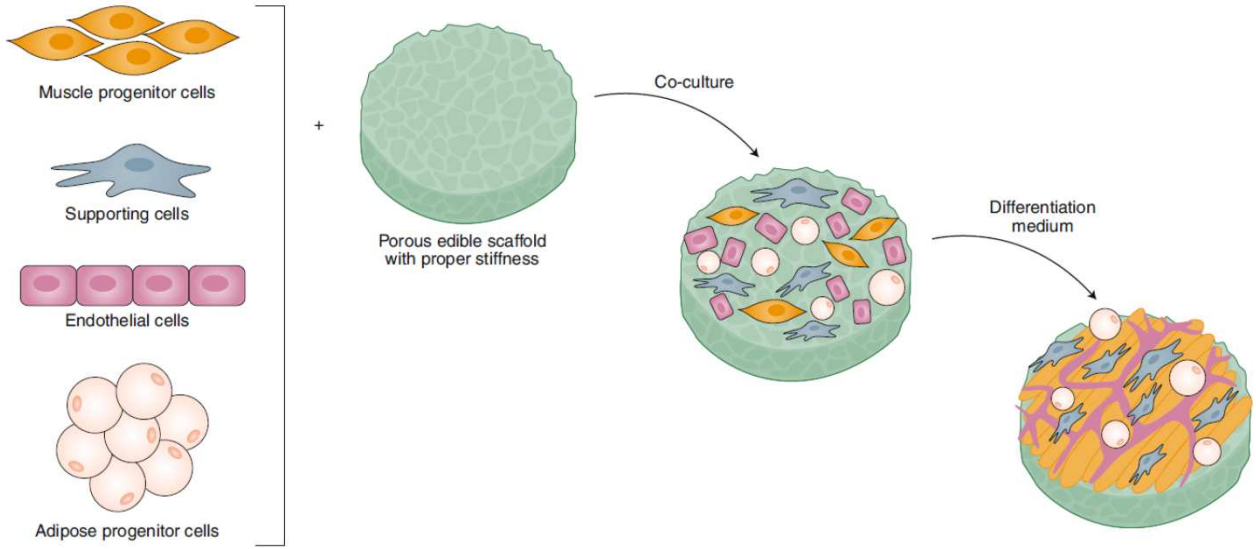
To mimic the structure of **livestock meat products**, whole-thickness tissues (composed of muscle, fat and connective tissue) need to be engineered, and so a more advanced technologies from tissue engineering, regenerative medicine, and biomaterials science to recreate the complex multicellular architecture of meat.

Complex tissues

Co-culturing different cells muscle fibres, adipose tissue and fibrous and vascular cells

Mechanical and/or electric stimulation to promote muscle contractility & stimulate production of myoglobin, responsible for the red colour

A perfusion system to deliver oxygen and nutrients and the effusion of metabolic wastes



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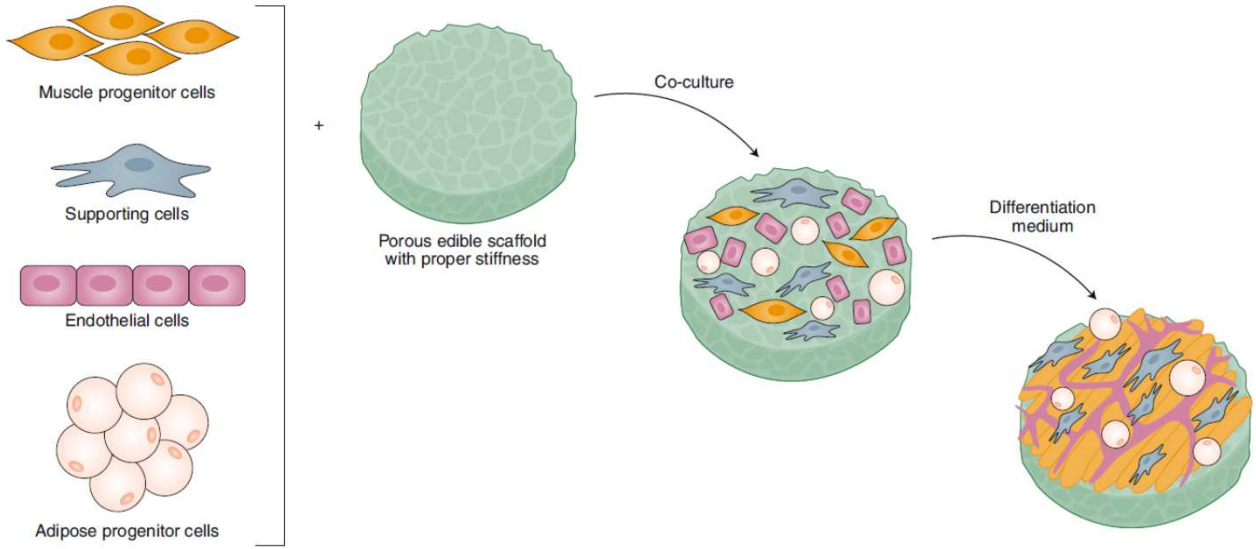
Scaffolds

Scaffolding is paramount for clean meat, as it provides the basis for structured, thick-tissue products that are more complex than simple ground meat mimics or cells used as ingredients

Scaffolding **can guide cell differentiation** either through its biomechanical properties or by physically anchoring specific signaling moieties or growth factors, or a combination of these approaches



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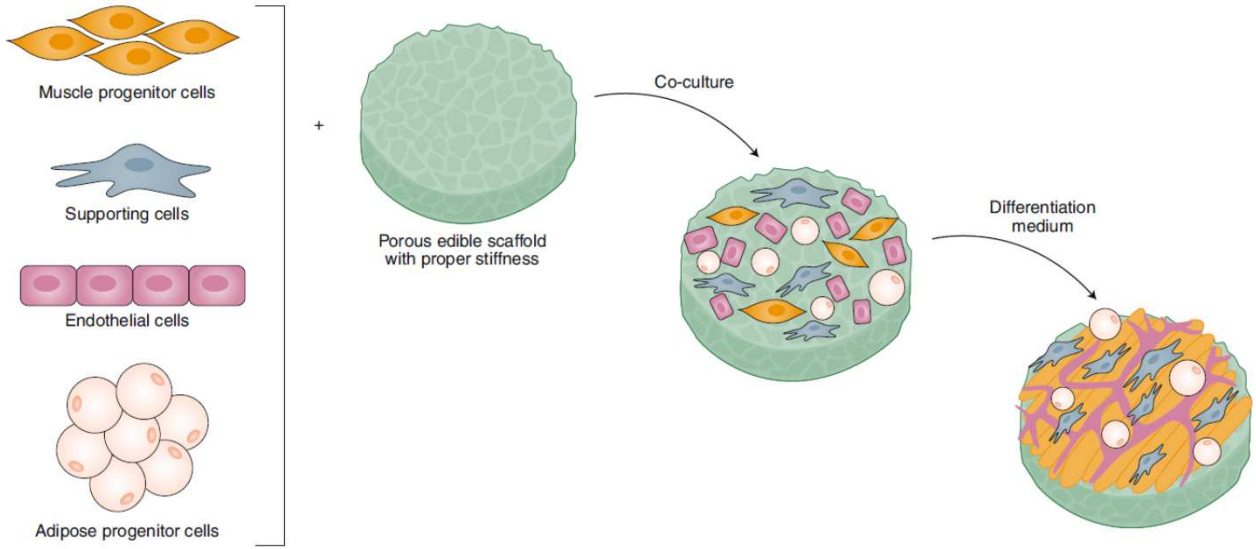
Scaffolds

This porous network allows **oxygen and nutrient** flow and **waste** product removal to maintain cell metabolic functions and avoid necrotic core formation.

Must fulfill specific **requirements** :

- ✓ Organoleptic properties, digestibility, thermal stability, water-binding capacity
- ✓ safe, economic and readily available for large-scale production



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Scaffold biomaterials

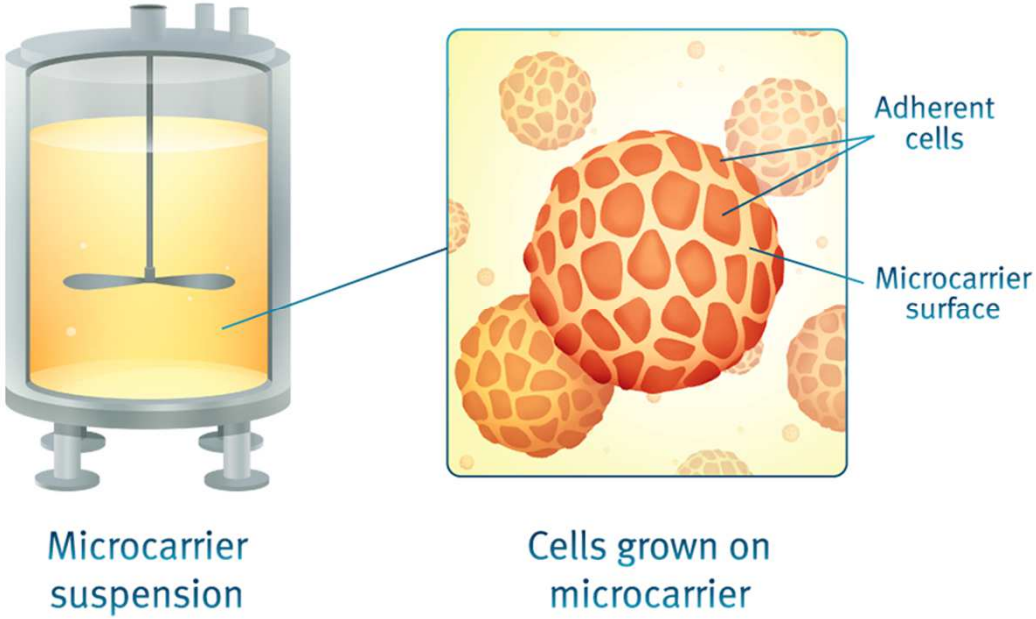
Natural biomaterials

- fibrin, laminin, hyaluronic acid, gelatin (i.e. hydrolyzed collagen), vitronectin,
- alginate, agarose and carrageenan from algae
- silk (from spiders), chitosan (from crustaceans, yeast, or fungi), plant cellulose, decellularized plant or animal tissues, fungal mycelium, textured soy protein
- lignin, pectin, gellan gum, glucomannan, starch, gluten,

Synthetic biomaterials

poly(ethylene glycol) (PEG), polyglycolic acid (PGA), poly(2-hydroxy ethyl methacrylate) (PHEMA), poly(acrylamide), poly (lactic-co-glycolic acid) (PLGA) and polylactide (PLA) (need to be functionalized or combined with natural biomaterials to support cell adhesion)

Scaffold biomaterials



Microcarriers

-permit attachment of cells

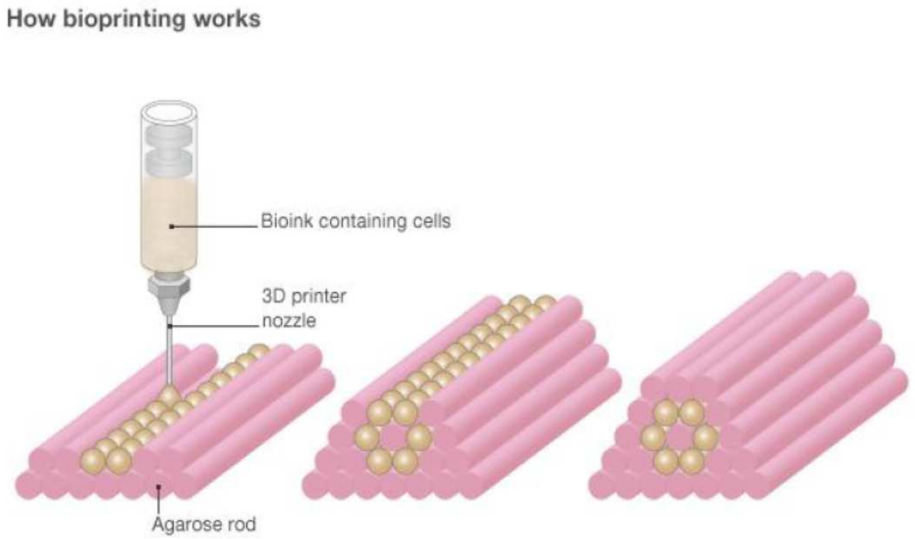
-provide a large surface area to volume ratio, permitting high densities of cells relative to 2D culture

Differentiation can occur on the microcarriers themselves triggered by changes in media components, microcarrier characteristics, or shear forces via mechanotransduction.

Source: https://elliot-swartz.squarespace.com/cellbasedmeat/cleanmeat301

Bioprinting

3D bioprinting is an additive manufacturing technique where pre-polymer solutions or pre-polymer solutions containing cells (i.e. a bioink) are deposited onto a substrate layer-by-layer under the guidance of a computer-aided design (CAD) process. The CAD files typically result from real bioimaging data such as magnetic resonance imaging (MRI) and computer tomography (CT) scans of tissues



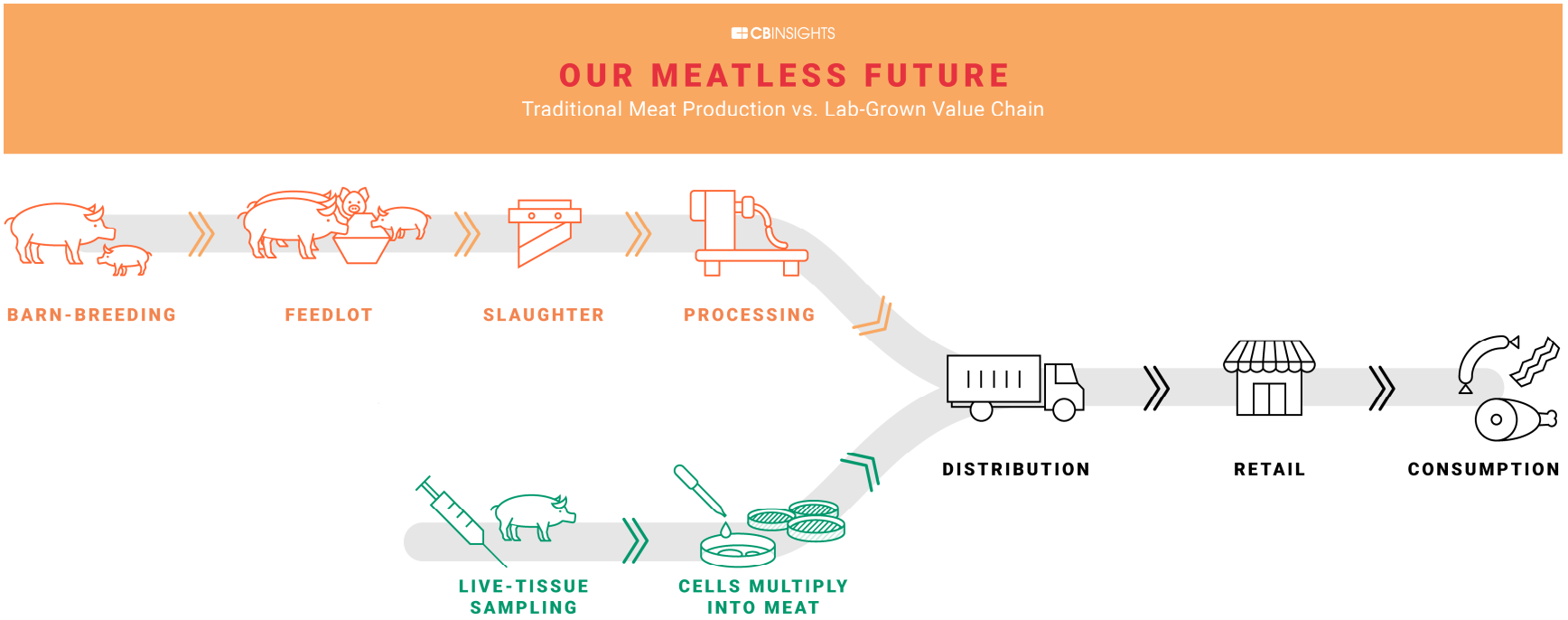
https://www.modernmeadow.com/

http://www.mexmads.com/carne-artificial-el-primer-corte-de-carne-impreso-en-el-mundo/

3. What are the benefits of Cultivated Meat?

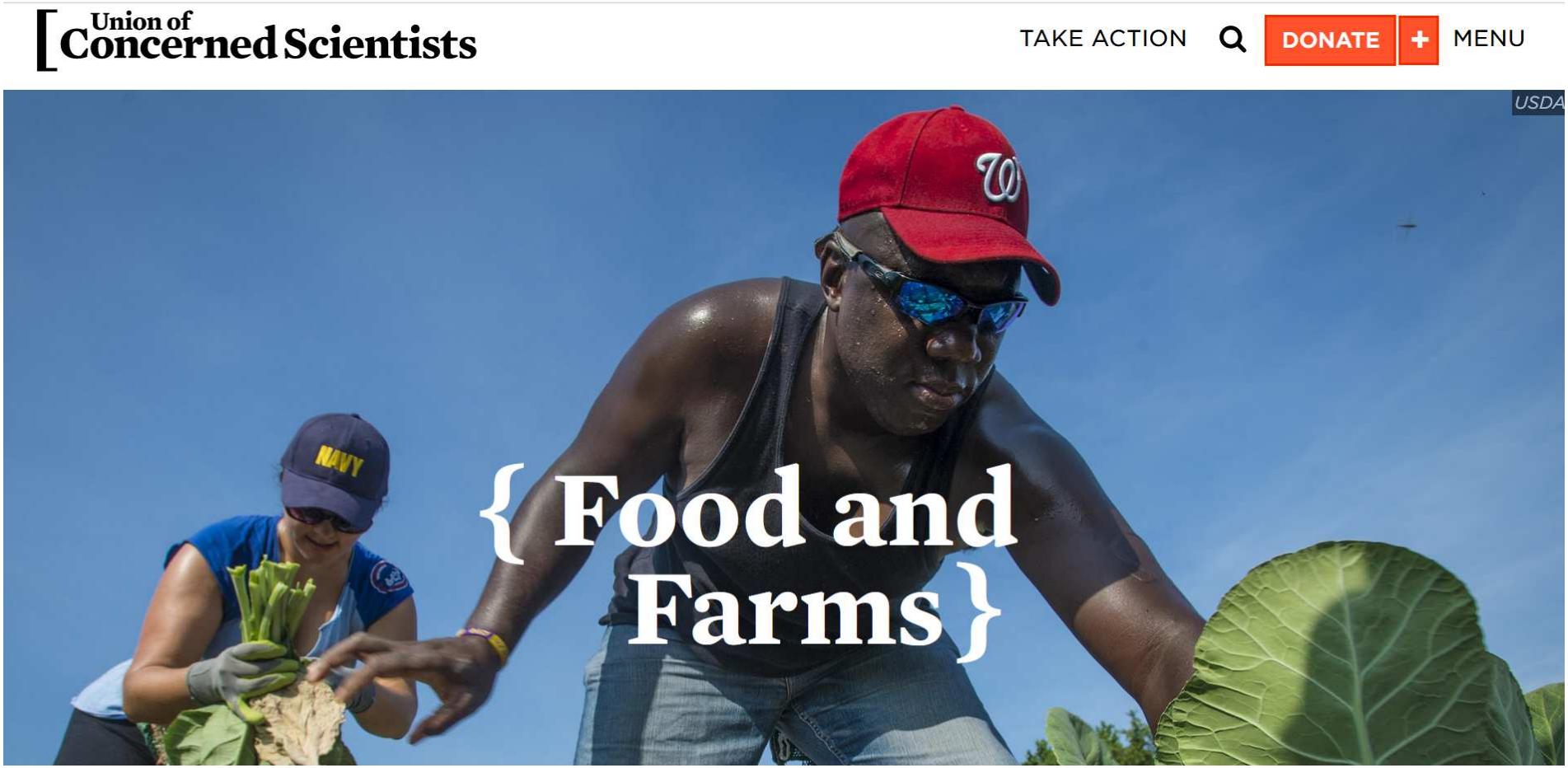
Advantages in terms of

Sustainability ?
Animal welfare ?
Public Health ?

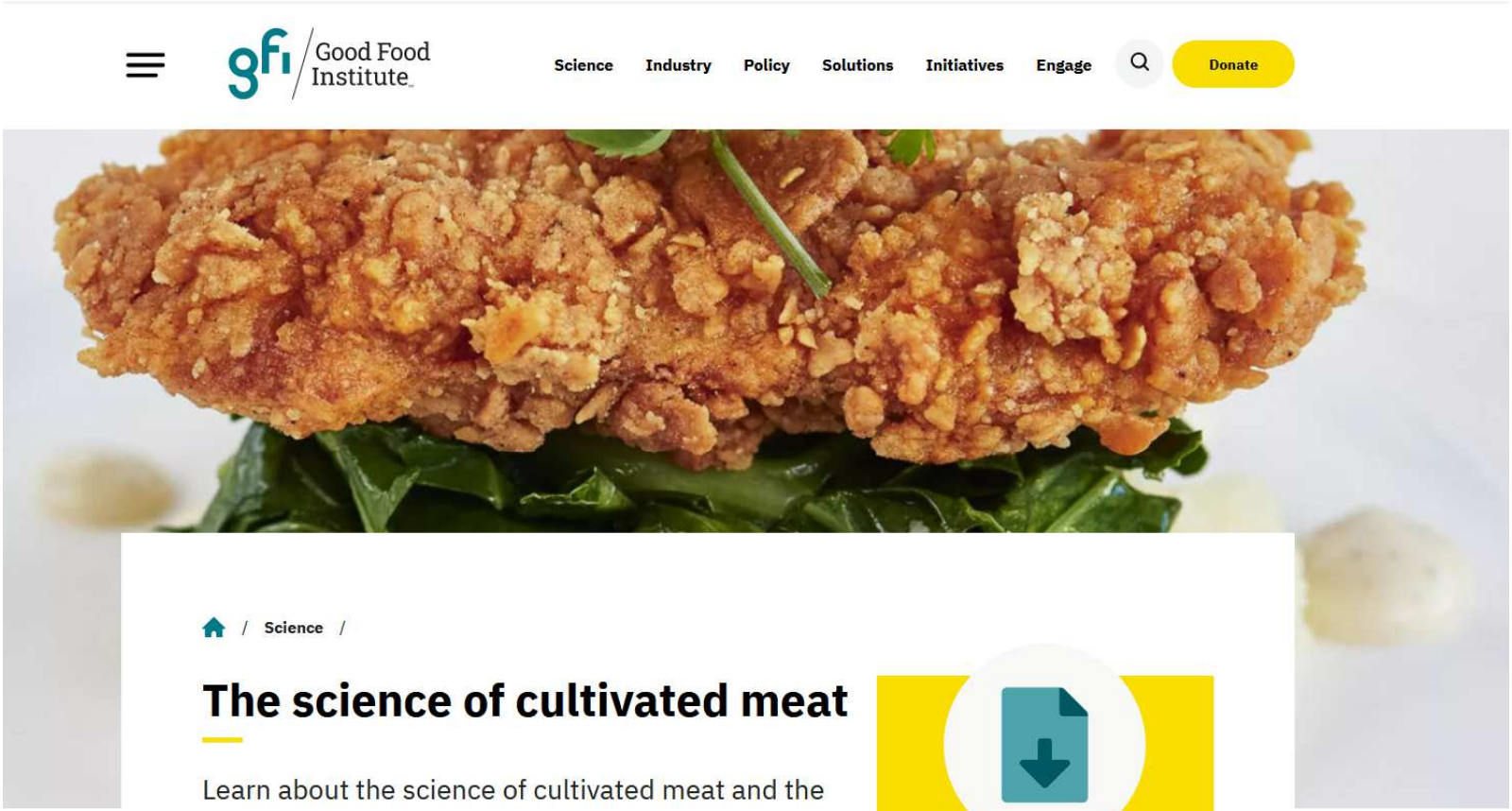


https://cbi-research-portal-uploads.s3.amazonaws.com/2017/11/08133451/110717-Our-Meatless-Future-Value-Chain-Comp-V3.png

https://www.ucsusa.org/food

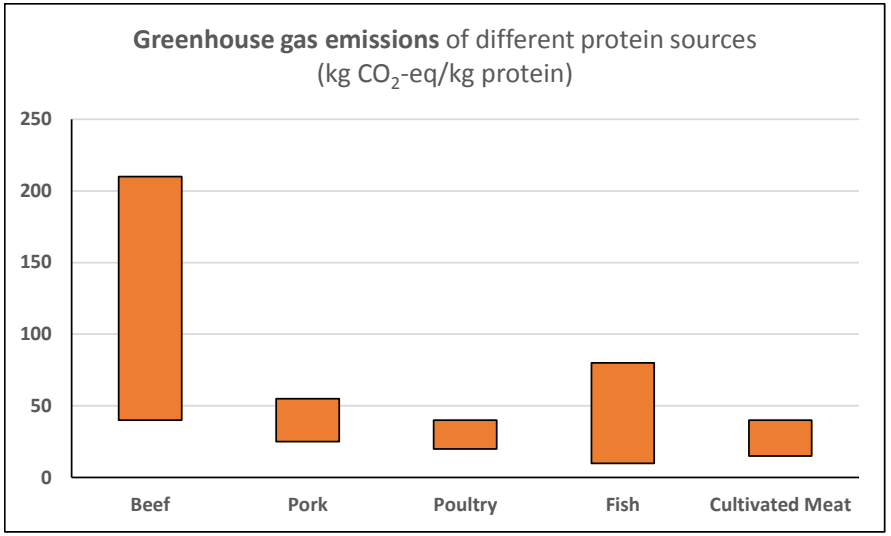


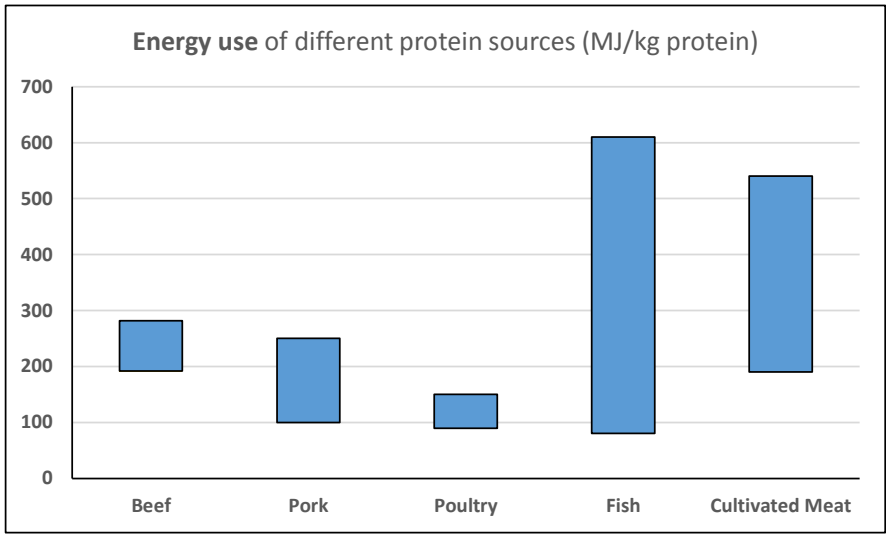
https://gfi.org/science/the-science-of-cultivated-meat/

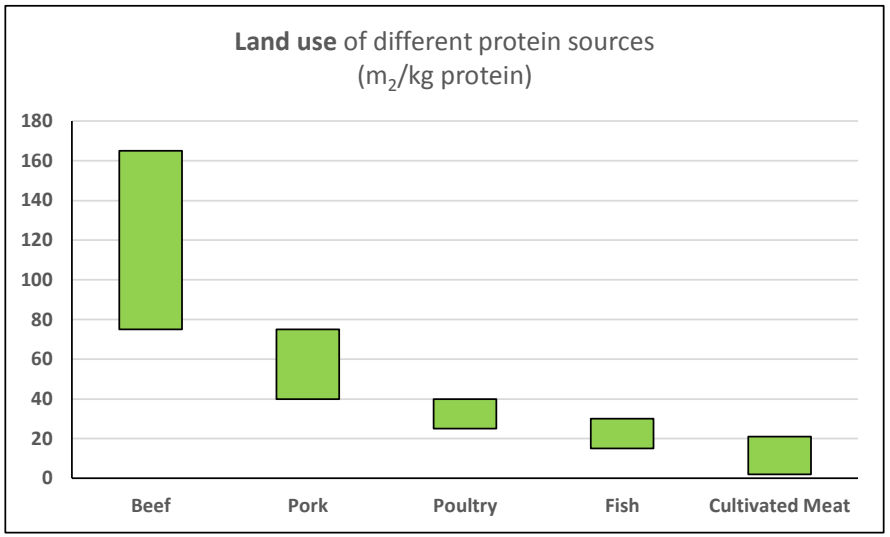


Sustainability of cultivated meat

No general consensus on the potential advantages in terms of GHG emissions of cultivated meat vs. conventional meat on a short-term or long-term basis







Sustainability of cultivated meat

Factors generating over-estimation of the impact

- Estimations based on currently available technologies & growth media
- Source of energy (low-emission energy sources decrease the impact)

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Factors generating under-estimation of the impact

- Management of meat industry wastes is a problem, but generates livestock co-products, such as leather, pet food, cosmetics, fertilizers, etc..

Sustainability of cultivated meat

Side-effects on biodiversity

a complete elimination of all livestock production is not reasonable from the perspective of biodiversity conservation

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Livestock play a role in a sustainable crop rotation system

clover-grass ley improves soil structure and increases soil carbon storage, and the plant fixes nitrogen from the atmosphere reducing the requirement for synthetic nitrogen fertilisers

Animal welfare

Approximately 56 billion animals are slaughtered for their meat every year.
One of the main purposes of cultivated meat is to stop the practices related to livestock growth and slaughtering.

Due to the lack of a nervous system, cultured cells and in vitro meat are supposed to be free from any type of pain although biopsies on animals to collect cells may raise some issues concerning animal welfare.

Cultured meat could be an attractive option for vegetarians, vegans, and opponents who reject meat consumption for ethical reasons

Whether painful or painless, animals must be reared so that their cells can be harvested to produce in vitro meat. "Consequently, lab-grown meat still involves animal exploitation, which is what the proponents f artificially grown meat want to avoid".

Public Health

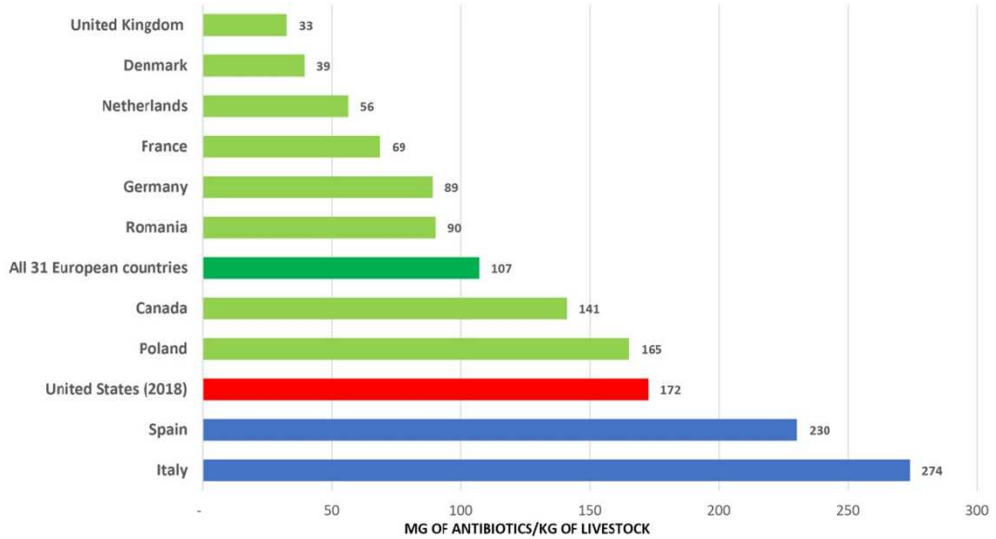
- ✓ Conventional meat is the most common food source of **potentially fatal infections,** such as *Salmonella* and *Listeria*

Source: https://www.nrdc.org/experts/avinash-kar/very-high-livestock-antibiotic-use-undercuts-effective-drugs

Public Health

- ✓ Conventional meat is the most common food source of **potentially fatal infections**, such as *Salmonella* and *Listeria*
- ✓ **Antibiotic abuse** in agriculture is a large problem that is contributing to antimicrobial resistance in human pathogens

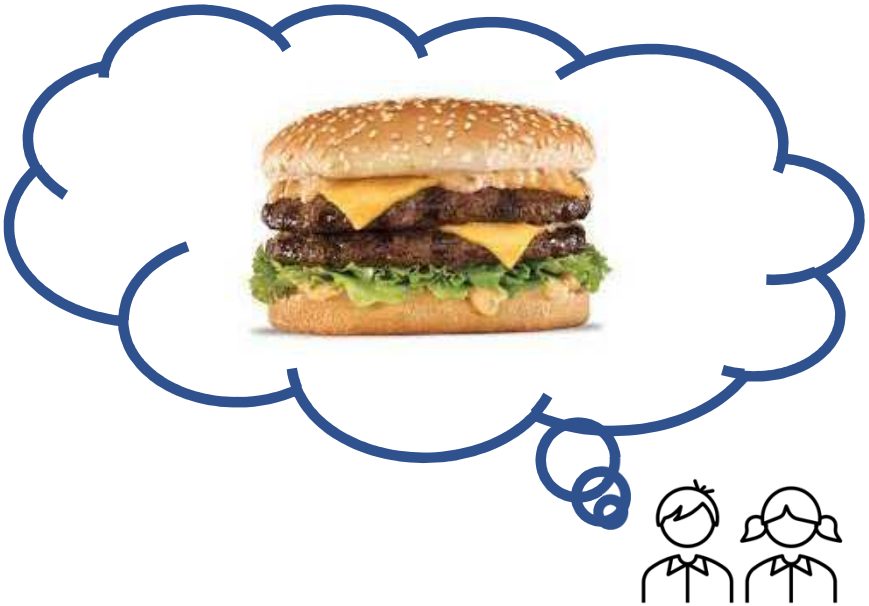
More than **6 million kg** of antibiotics were sold for livestock in 2018, compared to about 3.2 million kg sold for human medicine in 2015

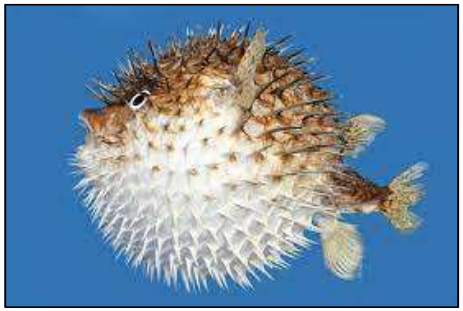


Source: https://www.nrdc.org/experts/avinash-kar/very-high-livestock-antibiotic-use-undercuts-effective-drugs

4. What are the differences from conventional meat?

Meat from unusual species





Nutritional properties

Traditional meat is a nutritionally dense food containing high-quality proteins, vitamins, minerals, and other important nutrients.

Many compounds that accumulate in the muscle are not produced in the muscle but **derive from animal feed components** which have been digested and modified by non-muscle organs.

Unless specifically added to the culture medium and taken up by the cells, these compounds would be absent in cultured meat, influencing processes determining flavor, texture, color and nutritional aspects.

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- ✓ **Macronutrient** (protein, lipids, fiber) composition and ratio of the overall product are affected by the scaffold material which typically largely exceeds the volume of the cells
- ✓ **Digestibility** of cultivated meat is still not well studied

- ✓ Level of **essential fatty acids** (mostly linoleic and alfa-linolenic acid) can be modulated
- ✓ **Minerals** (Fe, Zn, Se) & **Vitamin B12**
  - -> level in the growth medium
  - -> post-culture addition

Organoleptic properties

- ✓ After slaughtering, meat is aged (~14 days) for **tenderization** and formation of flavour precursors

- ✓ The tenderization process is complex, involving many proteolytic enzymes and has been studied for many years but is not entirely elucidated there is **no information available on whether and to which extent such transformations occur in cultivated meat**

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- ✓ **The red colour** of meat is mainly attributed to the presence of myoglobin, a heme containing protein. Cultured muscle tissues generally have **a pale colour** due to the absence of myoglobin, since myoglobin expression is suppressed at ambient oxygen conditions.

  Possible solutions

  -increase of iron level in growth medium

  -direct addition of myoglobin or other colorants (soy leghemoglobin) to the medium

Organoleptic properties

Fresh, uncooked meat has little **flavour**. It tastes rather bloody which is attributed to its relatively high iron content. Other compounds contributing to the taste are lactate (sour taste) and inosine 5'-monophosphate (IMP, umami taste), **both formed during post-mortem metabolism.**

Upon heating, complex **thermally-induced reactions involving precursors** (Maillard, PUFA degradation) generate a large number of volatiles, some of which contribute to the typical meat flavour. In traditional meat, substantial amounts of these precursors **are formed during post-mortem metabolism**

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On the other hand, some specific problems related to **off-flavours** that occur in some traditional meats can be avoided.

An example is **boar taint**, an off-odour present in uncastrated male pigs, related to the presence of androstenone, indol, and skatol.

Safety issues

Reduced risk of zoonotic diseases (if animal donor is pathogen free)
Environment fully controlled, low microbial contamination (e.g. *E. coli*, Salmonella, Campylobacter)

BUT **there are big gaps in the current knowledge of food safety of the whole process**

Animal serum in the culture medium -> virus, prions
Use of genetic engineering (*e.g.*, generation of iPSCs)
Contaminants in culture medium
Residues of hormones and growth factors used to sustain cell (higher than usually found in meat)
Dysregulation of cell lines
Accumulation of metabolites
Use of antibiotics
Undifferentiated cell lines resemble cancer & could cause disease in immune suppressed people

5. What about social issues?

Religion

✓ **Judaism ->** Kosher if cells coming from a kosher-slaughtered animal

✓ **Islam –>** Halal if the cells used are from a halal-slaughtered animal and no blood or animal-based serum is used in the production process (but not pig in any case…)

✓ **Hinduism ->** good acceptability following the principle of nonviolence (but not in the case of beef/cows)

✓ **Buddhism ->** majority would eat cultivated meat

Regulation

Authorization & Safety
-U.S. Department of Agriculture (**USDA**) and the U.S. Food and Drug Administration (**FDA**)
-EC, following the opinion of EFSA (Novel Foods Regulation & GMO legislation)

Identity of the product
-(USA) cell-based meat and poultry products are 'meat' and 'poultry products'
-(EU) Pressure from meat industry stakeholders to ban the term "meat" for cultivated meat products

Meat is defined as "skeletal muscles of mammalian and bird species recognized as fit for human consumption with naturally included or adherent tissues."

Skeletal muscle is defined as "muscles under the voluntary control of the somatic nervous system."

Ongoing debate regarding the use of the terms "steak", "sausage", "escalope", "burger" and "hamburger" for non-conventional meat products.
Certain meat products have protected legal names under national legislation, such as "tartar"

Socio-Economic dimension

Concerns about

-impact of cultivated meat **on local food systems**, farmers communities, slaughterhouse, equipment manufacturer, etc..

-shifting power in the food system

-consolidation of strategic food production under large corporations (**oligopolies**)

-price and social inequality
wealth and status vs. commonplace

6. When will Cultivated Meat make it to market?

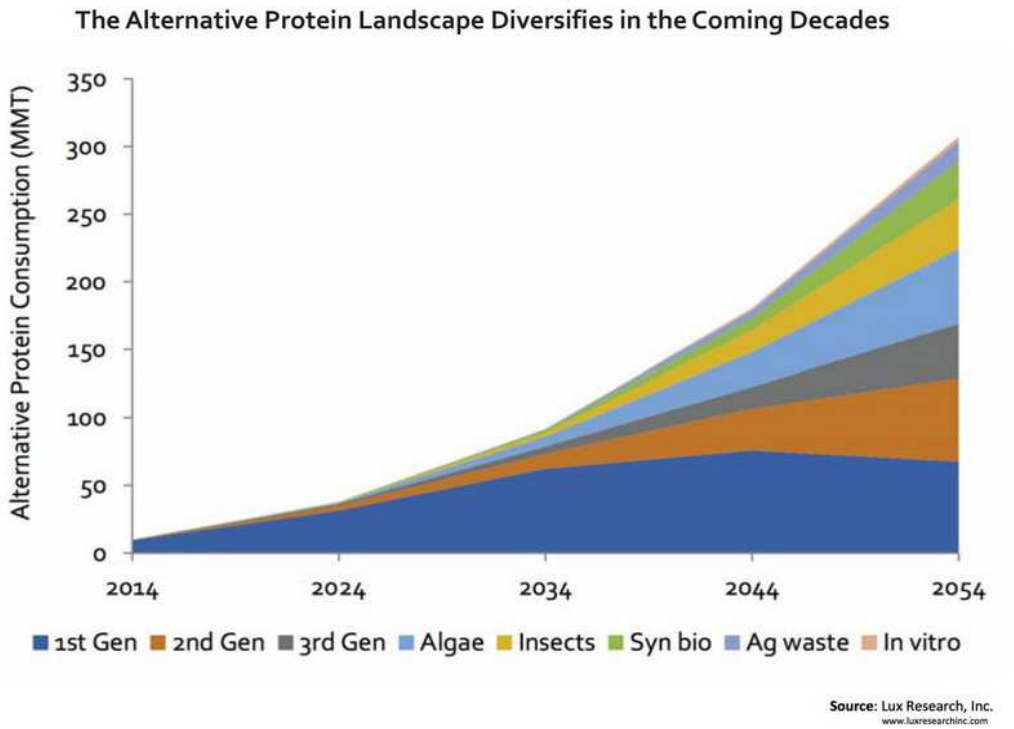
…it's already on the market!

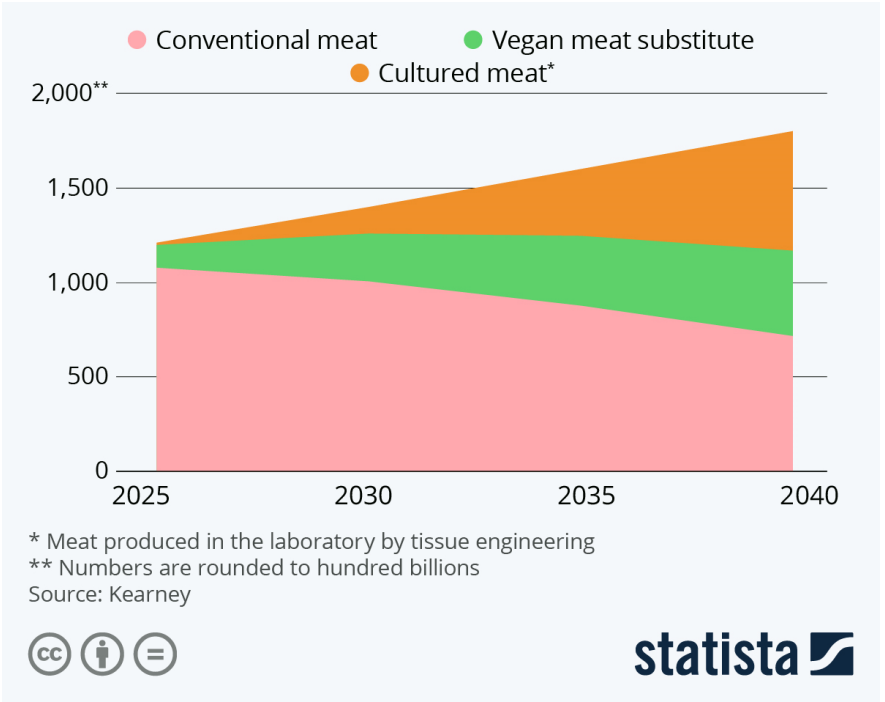
Receipt from the first consumer sale of cultivated meat. Singapore restaurant 1880 added Eat Just's *GOOD* cultivated chicken bites to the menu in December 2020. | Image credit: Eat Just

GFI – 2020 State of the Industry Report Cultivated meat

Evolution of the predicted alternative protein landscape

2015 **vs.** **2020**

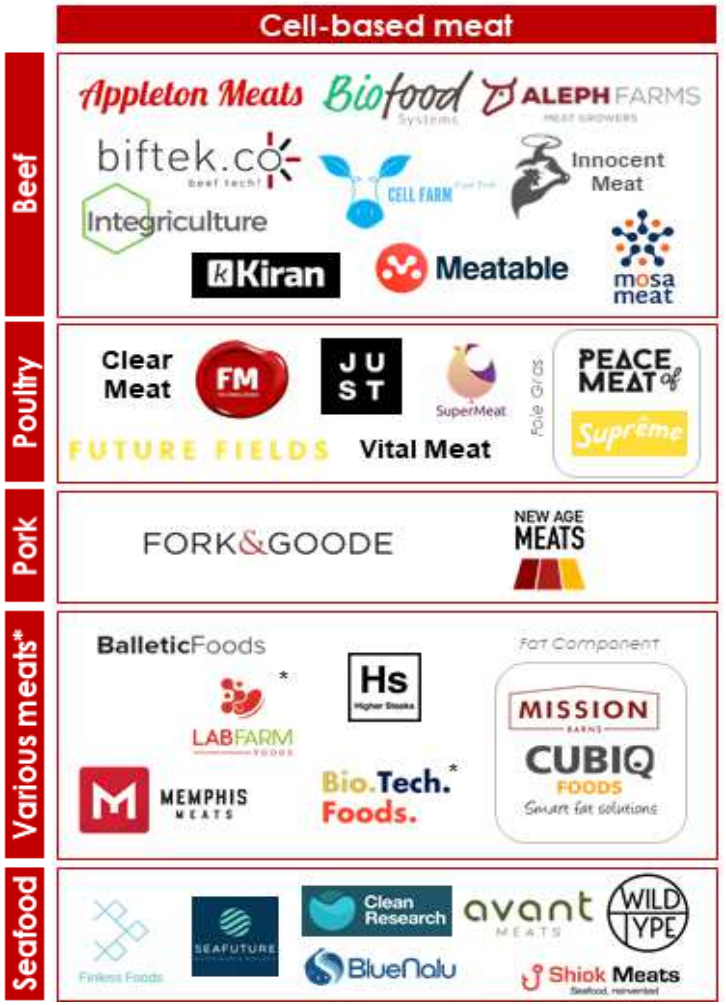




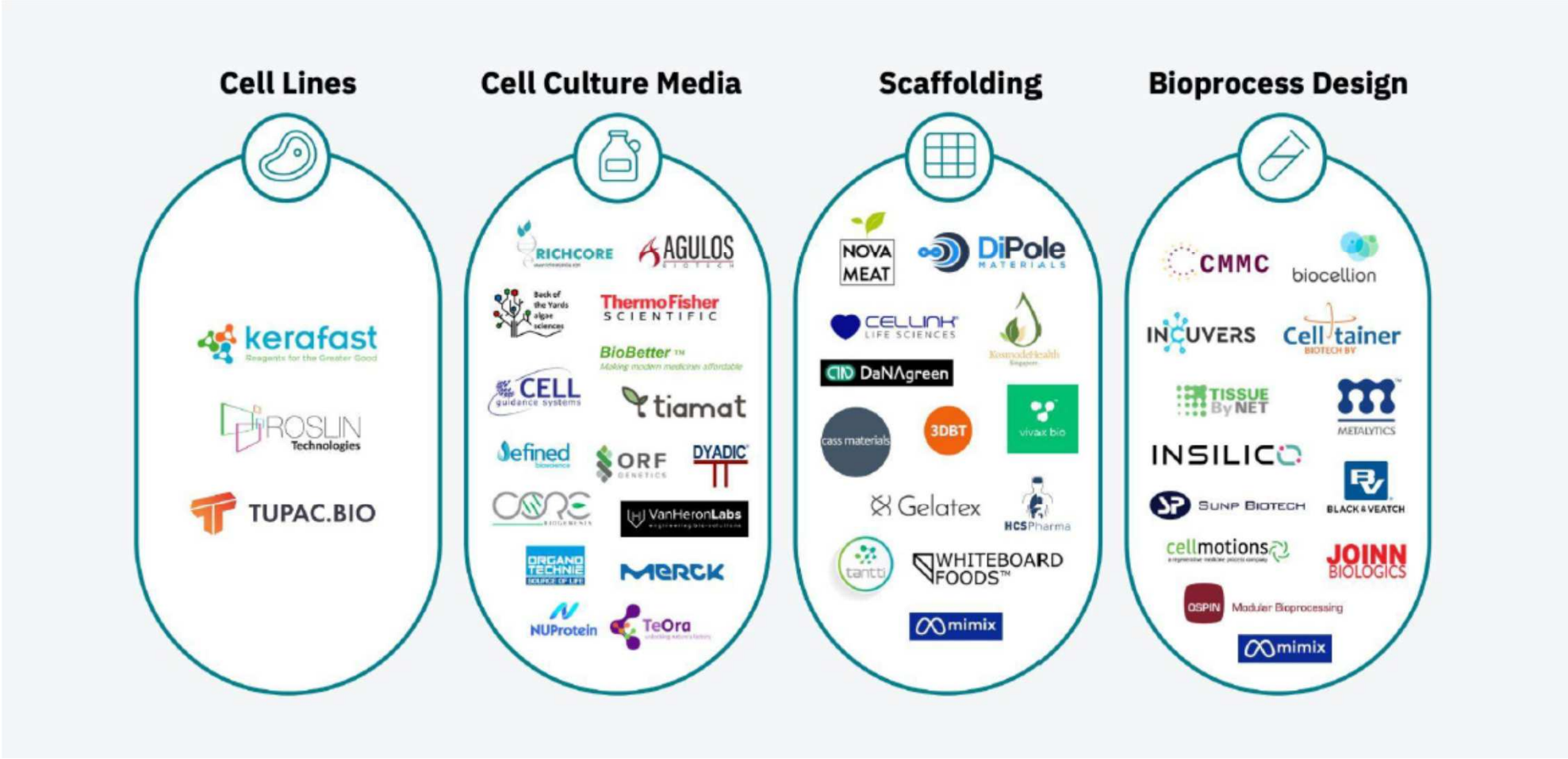
https://www.statista.com/chart/20464/global-meat-consumption/

Companies

JUST	2011, USA
Mosa Meat	2015, NL (*Nutreco, Merck*)
IntegriCulture	2015, Japan
(Menphis Meat)	2015, USA (*Tyson & Cargill*)
ALEPH FARMS	2016, Israel
BlueNalu	2017, USA (*Nutreco*)
Bio.Tech. Foods.	**2017, San Sebástian**
CUBIQ FOODS	**2018, Barcelona**

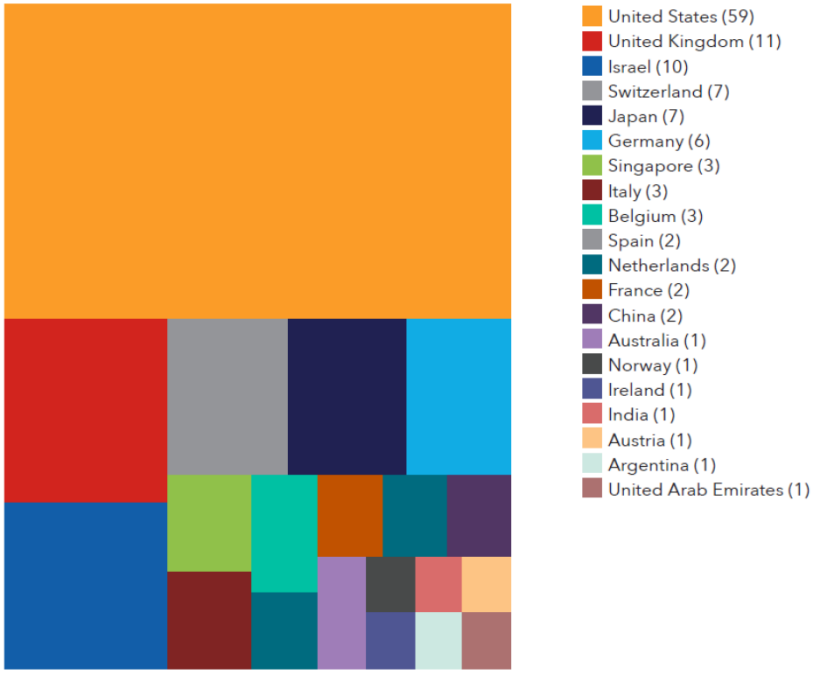


Commercial ecosystem

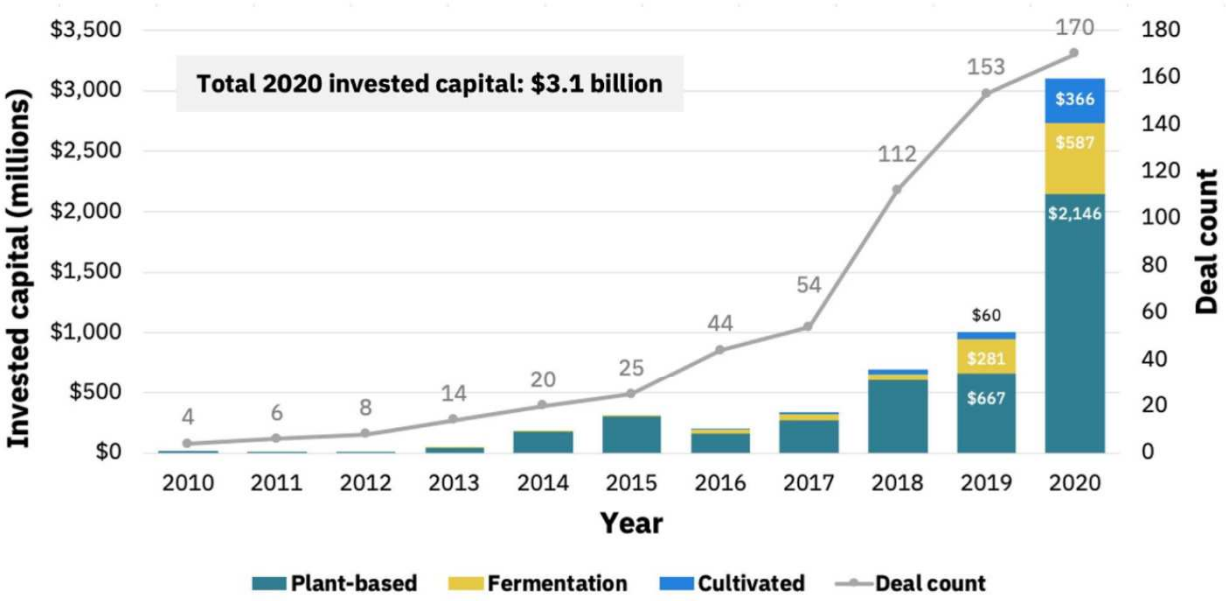


Investments

Top Investing Countries



Annual alternative protein investment backdrop



Source: GFI analysis of PitchBook data. *Note*: Data has not been reviewed by PitchBook analysts.

PitchBook

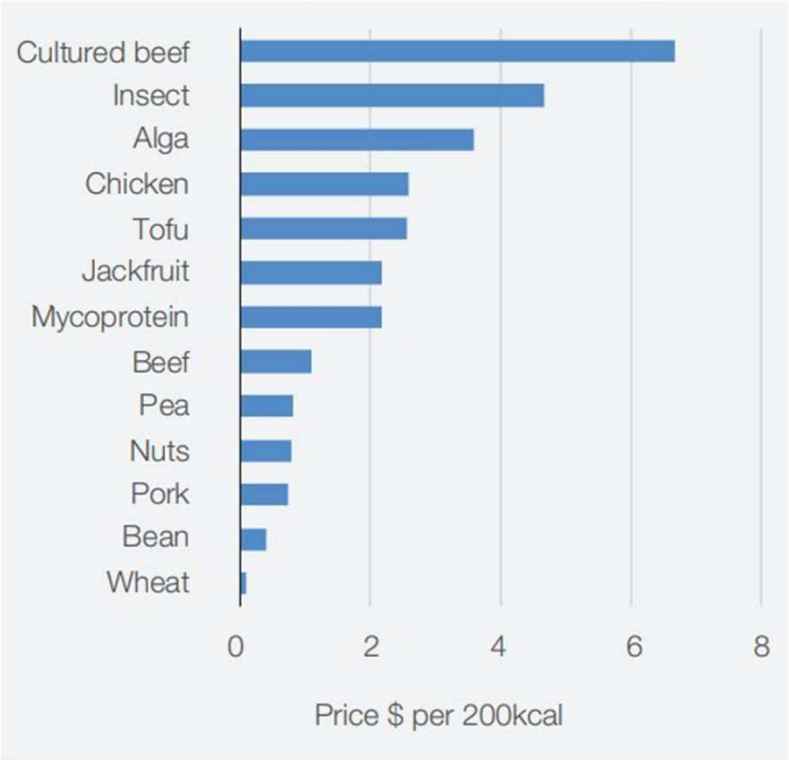
The Good Food Institute - 2020 State of the Industry Report Cultivated Meat

Limiting factors, barriers & constraints

- Price

Technologies for culturing of animal cells as food ingredients are still at the research stage, and scaling up the processes for commercial production requires major investments in R+D.
In the next few years, we can likely expect to see the cost of lab-grown meat decrease considerably.

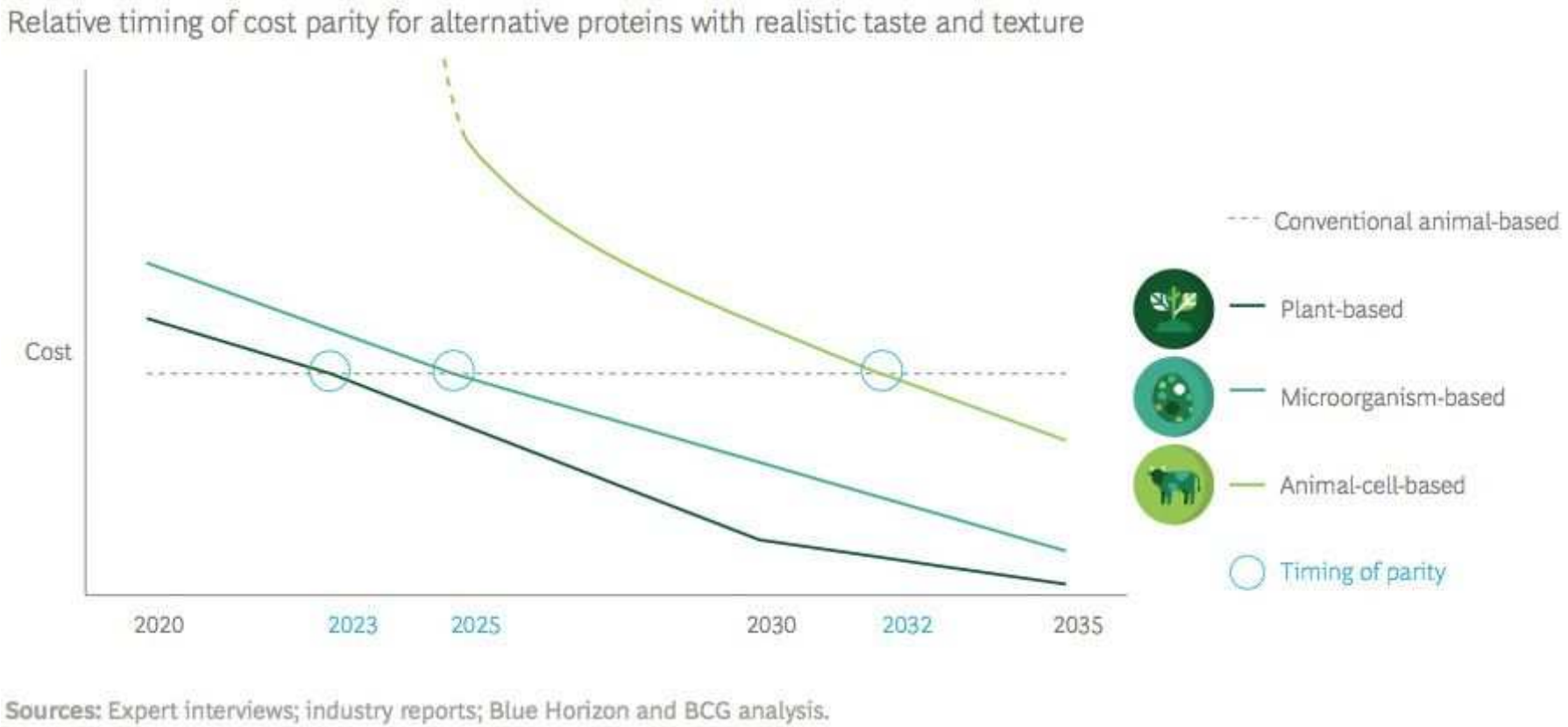
In 2019, about one in three U.S. consumers say they are likely to regularly purchase cultivated meat, and about one in five respond that they **are willing to pay a higher price** for cultivated meat than for its conventional counterpart.
Dutch consumers indicate that they are willing to pay nearly 40% more.



https://www.ipsingredis.com/media/2508/ips-ingredis-industry-insight-global-sustainability-through-alternative-proteins.pdf

Limiting factors, barriers & constraints

- Price



https://www.consultancy.eu/news/6348/alternative-proteins-a-potential-290-billion-plus-market-by-2035

Limiting factors, barriers & constraints

-Price

-Consumer acceptance

Consumer acceptance is a necessary for commercial success of cultured meat in the short term

Survey data are inconsistent, and attitudes depend on a number of factors, including the phrasing of the question and the nationality of the sample and the amount of information given to the survey participants

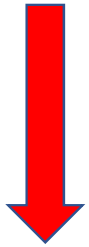
Cultured meat **is more appealing to consumers in America and Asia** than to those in Europe

Consumer acceptance **could depend on the information** people are exposed to — media coverage of cultured meat thus far has been largely positive

Consumer acceptance

Drivers at consumer level influencing the growth of the cultivated meat space

"Cultivated/clean meat"
Sustainability
Animal welfare
Health and wellness
Uniqueness & novelty
Adaptability & convenience
Gender (men)
Young people
Religion



"Lab-meat"
Considered a technology product rather than meat
Scepticism regarding safety & nutritional value
Transparency about the production process
Benefits unclear
Gender (women)
Elder people

Limiting factors, barriers & constraints

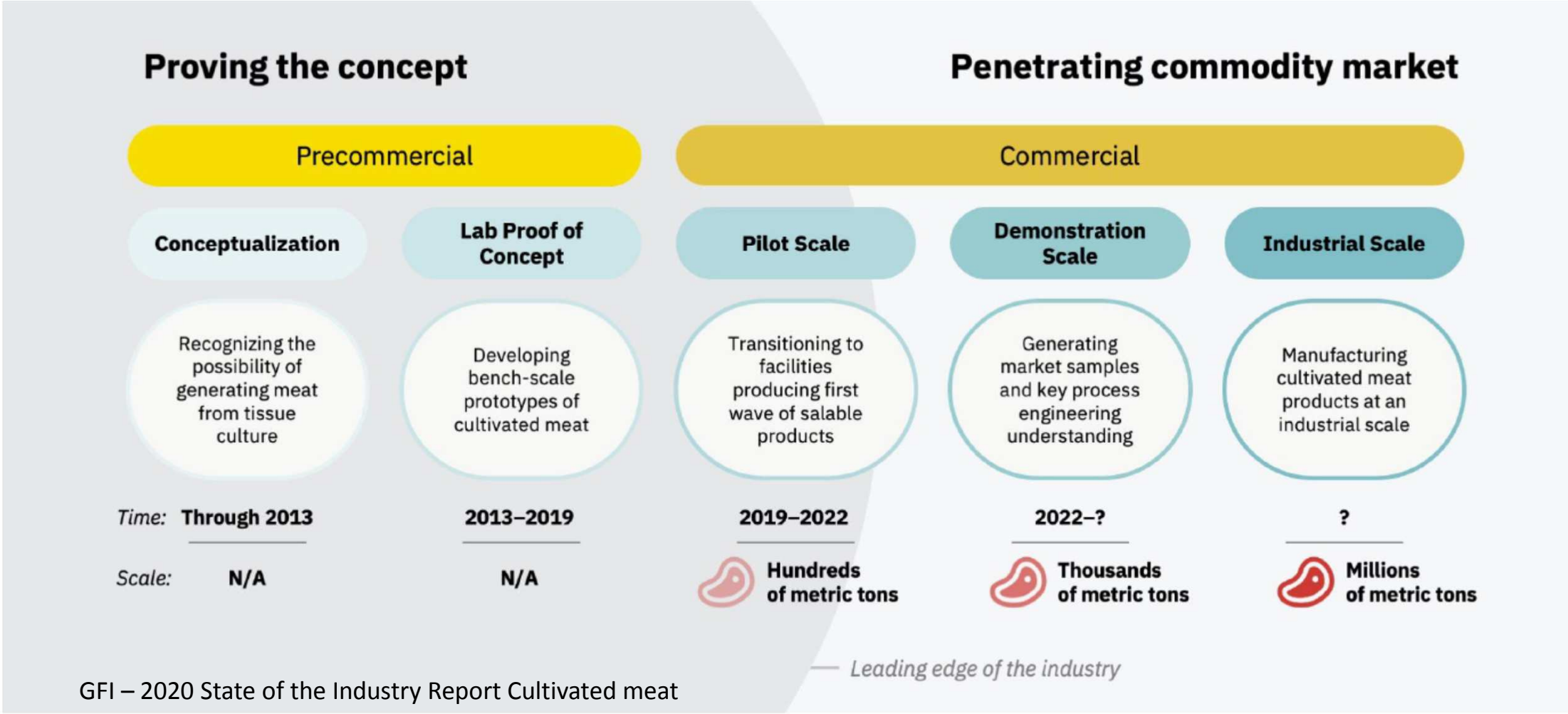
-Price
-Consumer acceptance

- Lack of established technologies/scale-up

Mind map of the critical technology sectors

Source: Specht et al., 2018; https://doi.org/10.1016/j.bej.2018.01.015

Technological readiness



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Limiting factors, barriers & constraints

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- Nutritional quality & Bioavailability

Limiting factors, barriers & constraints

-Price
-Consumer acceptance
-Lack of established technologies/scale-up
-Regulation, legal framework, labelling
-Religion, ethics
-Allergies & safety issues
-Nutritional quality & Bioavailability
- Organoleptic & functional properties

Limiting factors, barriers & constraints

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-Organoleptic & functional properties
- Supply chain issues

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-Supply chain issues

- Local preferences

Limiting factors, barriers & constraints

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-Organoleptic & functional properties
-Supply chain issues
-Local preferences

- Sustainability (land/energy/water use)

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-Religion, ethics
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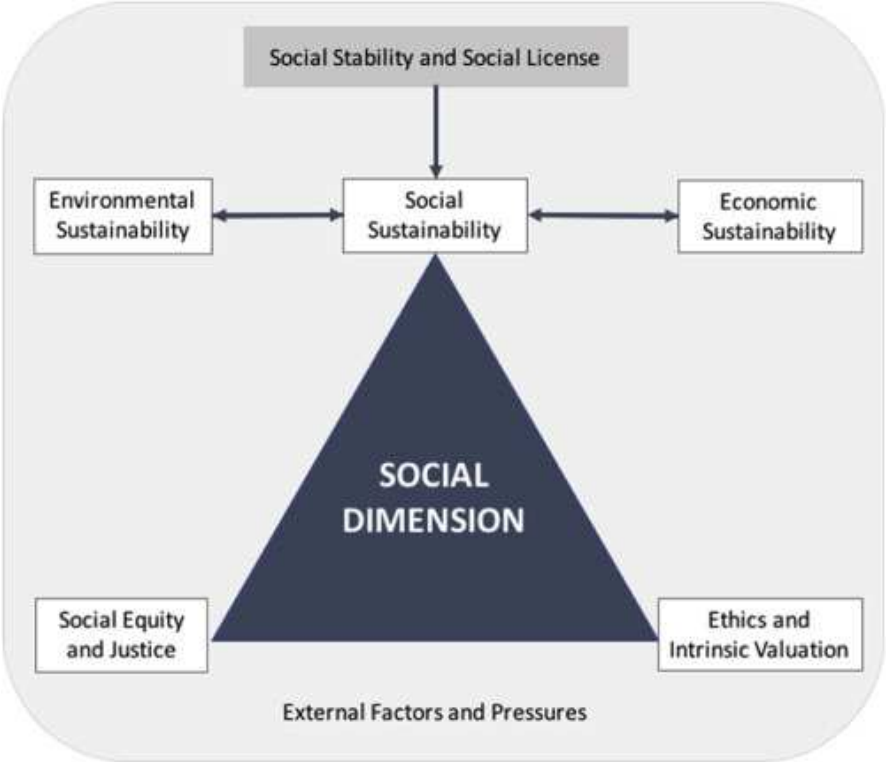
-Organoleptic & functional properties
-Supply chain issues
-Local preferences
- Sustainability (land/energy/water use)
- **Social dimension**

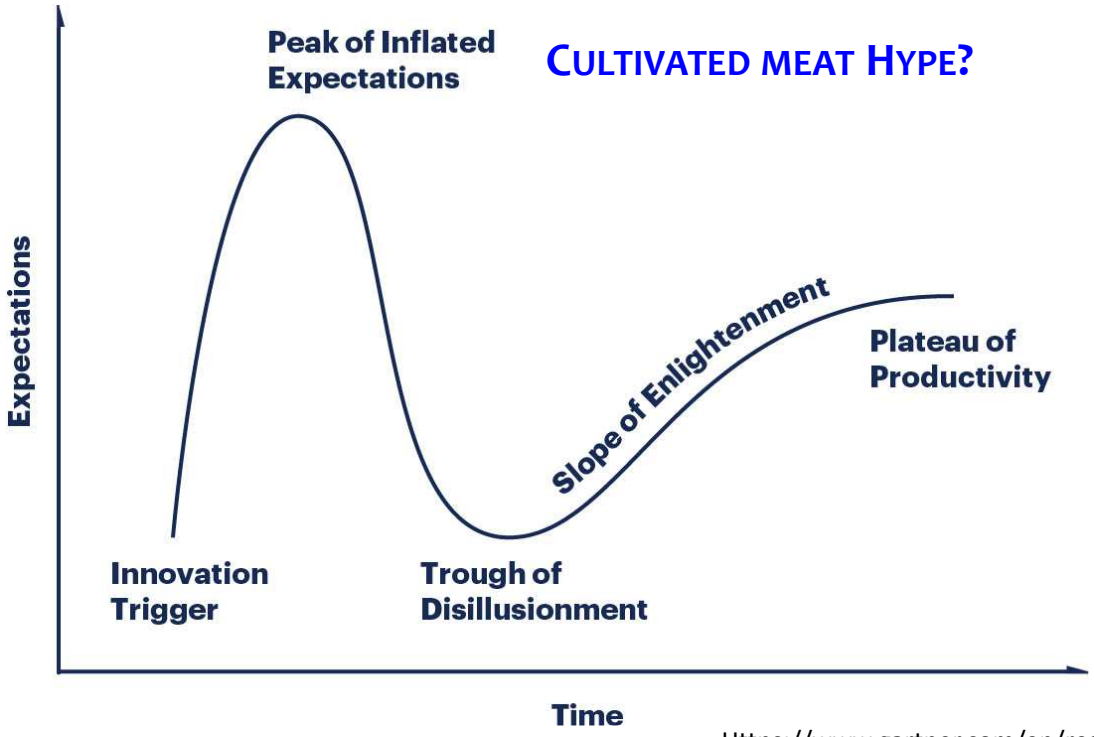


Grimmel et al., 2019. ttps://doi.org/10.1016/j.ocecoaman.2019.02.013

Take-home message

Take-home message

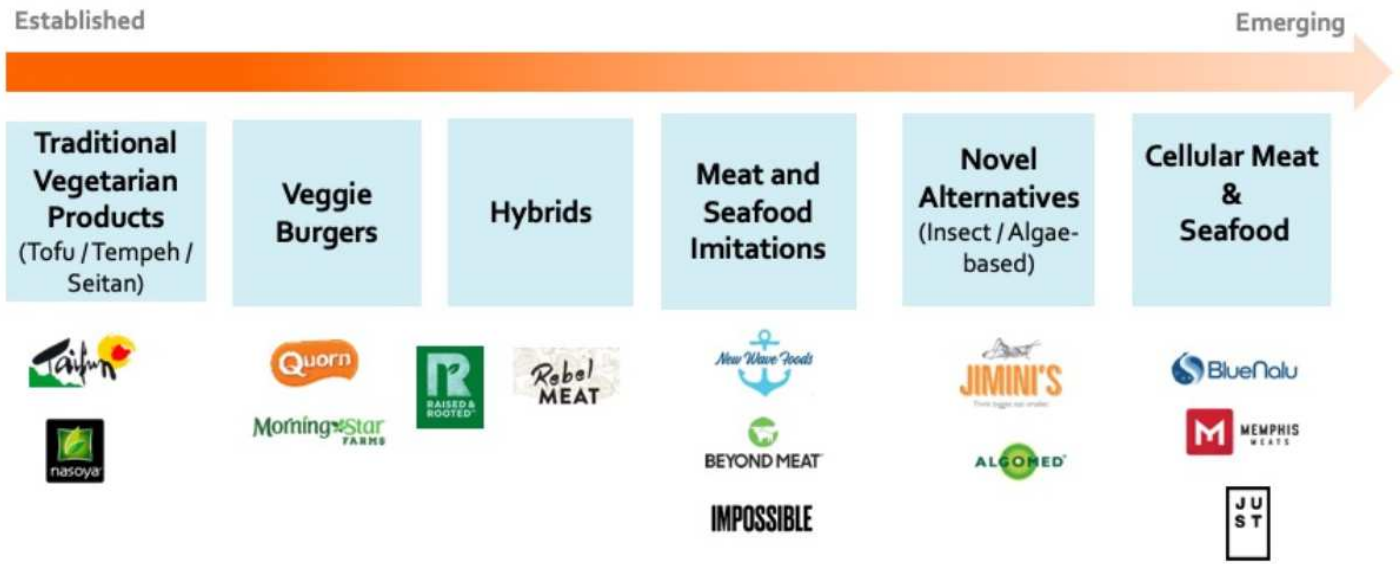
- Disruptive technology, great potential impact



Https://www.gartner.com/en/research/methodologies/gartner-hype-cycle

Take-home message

- Disruptive technology, great potential impact
- Need for more core science & technological improvements in many steps of the process as well as for its industrial scale-up



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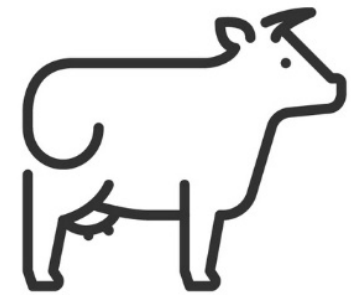
- Environmental benefits and safety of cultivated meat must be further investigated

Take-home message

- Disruptive technology, great potential impact
- Need for more core science & technological improvements in many steps of the process as well as for its industrial scale-up
- Cultured meat currently differ significantly from traditional meat in its technological, sensorial and nutritional properties
- Cost issues
- Environmental benefits and safety of cultivated meat must be further investigated
- Regulatory & labelling aspects still not clear

Take-home message

All protein sources inherently contain both drawbacks and advantages that will affect their sustainability, as well as their ability to be commercialized and accepted by consumers



Web page
https://elliot-swartz.squarespace.com/cellbasedmeat/cleanmeat301

Relevant literature

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Post M.J., et al. (**2020**). Scientific, sustainability and regulatory challenges of cultured meat. https://doi.org/10.1038/s43016-020-0112-z

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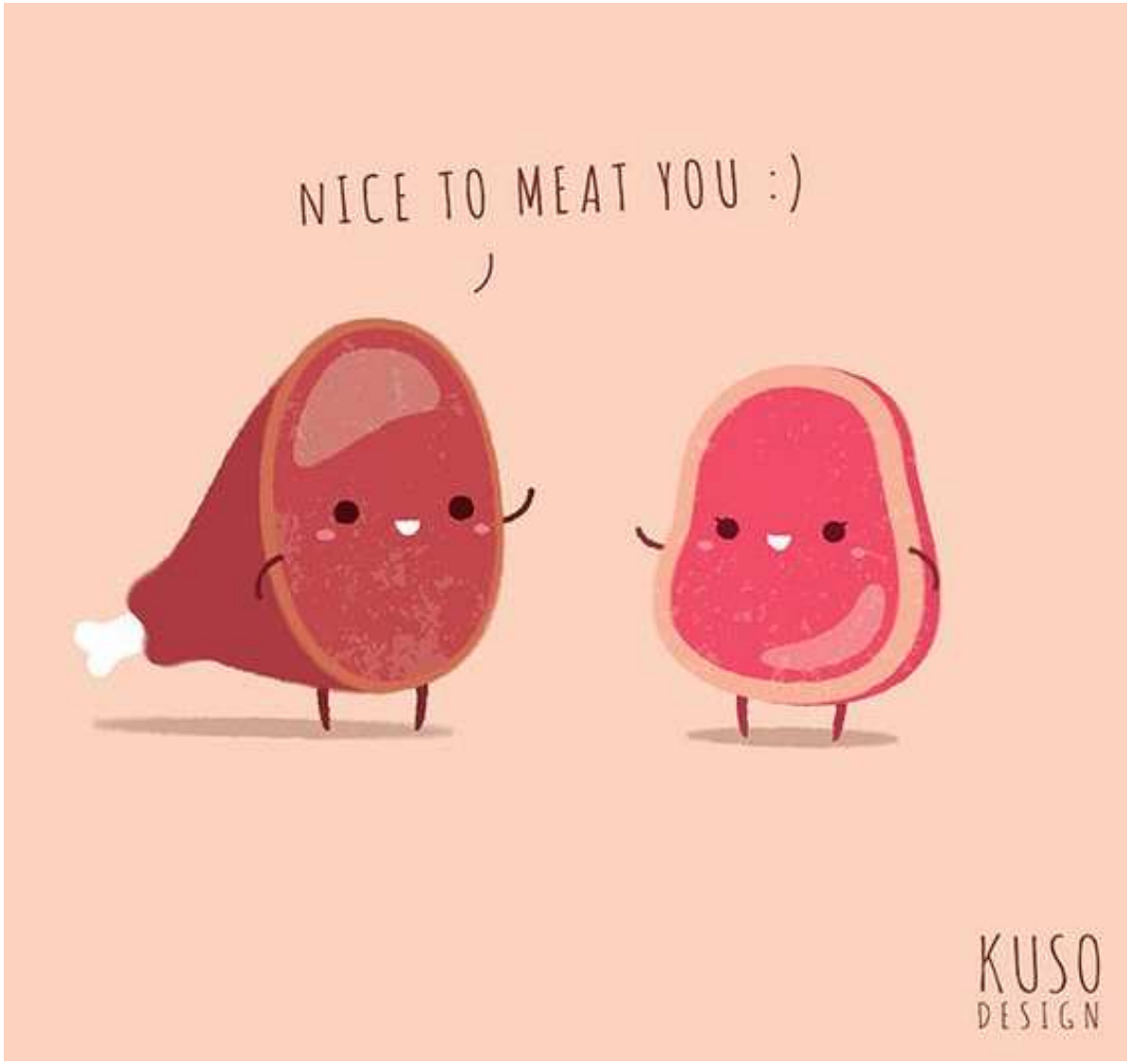
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