

# A menu of policy options for UK R&D to advance research and commercialisation of sustainable proteins in the UK

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# **1.** The case for more R&D funding for sustainable proteins in the UK

Making meat from plants and cultivating it from cells presents enormous opportunities to provide the British public with the familiar foods they love, but at a fraction of the external cost on the environment and planetary health. Plant-based meat production <u>emits</u> up to 90% fewer greenhouse gas emissions and uses up to 99% less land than conventional meat. When produced with renewable energy, cultivated meat <u>could cut</u> the climate impact of meat by 92% and use up to 95% less land. In addition, these sustainable proteins are free of antibiotics, and involve no risk of the emergence of zoonotic diseases, as is <u>associated</u> with raising and killing animals for food.

The government's <u>Net Zero Strategy recognises</u> that the UK is exceptionally well-placed – given its world-class scientific expertise in relevant fields and enthusiastic consumer base – to establish a leadership role in the sustainable protein space. Doing so would align with many of the UK's existing policy commitments: including reaching net zero by 2050, effective containment of the looming threat of antimicrobial resistance by 2040, and establishing its reputation as a global scientific superpower. It is also clear, given the projected growth in this space in the coming decade, that the UK would reap enormous economic and reputational benefits from doing so.

However, GFI's <u>own work</u> based on mapping the allocated funds and speaking with experts in the field have highlighted several barriers in the UK's R&D ecosystem that mean the UK is currently failing to meet its potential, and is falling behind other countries. Ambitious and forward-looking policy is needed now, so that the UK can capitalise on its existing strengths, realise the clear societal benefits, and embrace the economic and commercial opportunities offered by this quickly-developing industry.

The UK should set out a clear ambition to become a global leader in the plant-based, cultivated meat and fermentation industries by 2027. This will involve developing a cross-government strategy, meaningfully investing in open-access research and development to advance the below priorities, ensuring a clear and robust regulatory framework, and creating a dynamic industry ecosystem.

# 2. A menu of policy options for UK R&D investment

As identified in our <u>research and industry ecosystem scoping exercise</u>, we consider that given the UK's highly relevant latent scientific strengths - even a relatively modest amount of research funding would allow the UK research community to make meaningful progress on a number of fundamental, pre-competitive R&D gaps in the sustainable protein space. The specific areas particularly suited to the UK's scientific strengths are identified in the next section.

Addressing these fundamental R&D gaps would not only would be beneficial for unlocking the transformative potential of sustainable proteins by bringing them closer to price and taste parity, but it would also allow the UK to leverage its existing advantages, build national capability in this field, and thereby position itself as a strong contender to capture a significant share of the projected economic growth in this sector.

We conservatively estimate that **£100m** in academic R&D funding, in combination with **£125m** for commercial development and infrastructure scale-up would allow the UK to make meaningful progress on the highest priority pre-competitive gaps identified below and cement itself as a competitive international player in the sustainable protein field.

### **STRAND 1: ACADEMIC R&D**

• **RECOMMENDATION: £100m** in academic funding would work out to the reasonable average of £2.7m for each of the 37 solution areas, which is in line with the level of funding granted to similar research projects in both the <u>plant-based</u> and <u>cultivated</u> space.

**INTERNATIONAL PERSPECTIVE:** In April this year the Netherlands <u>invested</u> almost £50 million towards developing a cellular agriculture ecosystem, as an initial step towards investing more than £300 million in total. In 2021 alone, Denmark invested nearly £150m, whilst Israel invested nearly £24m into cultivated meat R&D. Our mapping has identified that the UK has fallen behind in terms of investment in relevant scientific areas relative to such countries for a number of years. With this backdrop, a £100m R&D commitment would give the UK a competitive edge on the international stage. A £50m R&D commitment - covering roughly half of the priority areas listed below - would ensure the UK does not fall further behind other countries.

THE COSTS OF INACTION: Without available funding, it is difficult to attract new talent to UK shores and yet more worryingly, the UK risks losing existing talent to other countries who are prioritising this space. As one academic put it to us: "Partnering with the likes of Singapore and America is probably an easier route for British researchers to get funding currently, so there is definitely a risk that UK researchers interested in this space will move abroad to pursue it." GFI's own Science and Technology Manager has spoken with many UK-based early-career scientists who are actively considering and pursuing opportunities abroad.

# STRAND 2: R&D RELATED TO COMMERCIAL DEVELOPMENT & INFRASTRUCTURE SCALE-UP

• **RECOMMENDATION:** A minimum of £125m for commercial development and infrastructure scale-up R&D activities would ensure the UK can translate some of the above foundational science into commercial advantage, and establish itself as an industry leader. As recommended in <u>the National Food Strategy</u>, this should comprise at least £50m to establish a new Innovation Cluster and £75m for start up grants over the next five years.

**INTERNATIONAL PERSPECTIVE:** Whereas little close-to-market innovation is happening in the sustainable protein space in the UK, by comparison some countries are prioritising the fostering of a dynamic research-industry ecosystem. For example, Israel's state-backed Innovation Authority launched two (Fresh Start and The Kitchen) of the country's 13 sustainable protein-related incubators and accelerators. In Singapore, the Government-backed research institute A\*STAR has fostered a number of joint public-private industry facilities, including a recent collaboration with Avant Meats for a new production facility for cultivated seafood, set to open in 2022. In this context, a £125m commitment for close-to-market R&D would bolster the UK's competitiveness internationally. A £50m R&D commitment - to establish the Innovation Cluster alone - would ensure the UK does not fall further behind other countries.

**THE COSTS OF INACTION:** A consequence of the lack of close-to-market innovation is that the UK research that is currently taking place is more likely to be commercialised abroad, rather than supporting the growth of British industry. This is not a distant possibility, but is already happening. For example, the research findings of a project led by the University of Cambridge was <u>acquired in 2018</u> by the Netherlands-based cultivated meat company Meatable, who have since raised over **\$170m** in funding rounds.

### Table 1: Breakdown of R&D policy options

Funding towards	Costing - options Ambitious vs Minimum needed to prevent UK falling behind		International examples
Academic funding to UKRI and specific universities build national capability; leverage UK academic strengths towards making key scientific breakthroughs	<b>£100 million</b> to allocate sufficient funding for progress on 37 high priority areas identified below	<b>£50 million</b> to allocate sufficient funding for progress on 18 high priority areas identified below	<ul> <li>In April 2022, the Dutch government announced a £50 million investment to develop the Dutch cellular agriculture ecosystem, an initial tranche of a potential total of £320 million.</li> <li>Denmark invested £150 million in plant-based R&amp;D in 2021.</li> <li>In 2021, Israel invested £13 million towards cultivated meat research consortium and the US announced £8 million to set up a <u>flagship research centre</u> for cultivated meat.</li> </ul>
Setting up an Innovation Cluster dedicated to ensuring UK research findings can translate into commercial success	<b>£50 million</b> in core funding to establish a cluster, with renewed funding (at least <b>£10</b> <b>million</b> <sup>1</sup> each year after the first five years)	<b>£50 million</b> to establish cluster	<ul> <li>The Canadian government has supported the establishment of the Protein Industries Canada supercluster, previously <u>allocating more than</u> £100 million to its establishing the cluster and <u>renewing this support</u> in its recent 2022 budget.</li> <li>As part of its £10 million investment towards the space, the Israeli Innovation Authority has established food-tech incubators such as <u>the Kitchen</u> and <u>Freshstart</u>, with significant alt protein representation in their portfolio</li> </ul>
Grants for start-ups	£75 million to maintain competitiveness with other countries	£10 million to ensure the UK does not fall further behind other countries (eg. Israel)	<ul> <li>The Australian public sector <u>committed</u>         £100 million towards a partnership         initiative to develop the infrastructure for         plant-based protein in South Australia.</li> <li>The Israeli Innovation Authority (the IIA)         has <u>invested</u> more than £10 million         towards direct investments into startups in         different stages (from early seed up to         manufacturing phases).</li> </ul>

<sup>&</sup>lt;sup>1</sup> This aligns with the level of funding needed for similar initiatives in related fields. For example the <u>UK's Cell and Gene Therapy Catapult</u>, set up in 2012, has received £70.6 million core funding over a five year period.

# 3. Sustainable protein R&D priorities with high suitability for UK scientific strengths

The proposals below represent a subset of high-impact opportunities that have emerged from <u>a</u> <u>GFI analysis</u> of the white spaces and innovation priority areas in the sector. Projects within the portfolio will have synergistic impacts, supporting the whole portfolio will therefore have a greater effect than the sum of each individual project and provide a greater return on investment. **The following priority areas have been identified as particularly well-suited to the UK's scientific and technical strengths:** 

## **Plant-based priority areas:**

The UK is home to world-leading expertise in the field of agricultural science, plant breeding, and plant biotechnology, with renowned institutes across the country including Edinburgh's Roslin centre, Aberystwyth University, Reading University, NIAB and the John Innes Centre. This expertise means the UK is particularly well positioned to undertake further exploration in analysing plant protein for functional use in plant-based meat, for example by addressing the following areas:

#### • Protein sequence, structure, and functionality database

There is a need for deeper fundamental research on the relationships between protein sequence, structure, functionality, and ultimately performance in plant-based food products.

#### • Plants as a recombinant protein expression platform for functional food ingredients

Microorganisms are typically used as recombinant protein hosts but more exploration is needed into the use of plants as expression platforms. This may yield a number of benefits: the use of plants as production hosts may require minimal processing into value-added ingredients, such as baking flour with integrated egg and dairy functional proteins. Plants offer ready scalability with less need for expensive equipment or downstream purification to isolate proteins of interest from inedible or undesirable hosts.

#### Biological processing methods for isolating protein ingredients

Processing crops into flours, isolates, and concentrates often relies on chemical and mechanical methods. Biological processing techniques may impart the desired composition and molecular structure for optimal functionality with increased precision, lower cost, and greater suitability for small-scale processing, but this needs further exploration.

## Fermentation priority areas:

The UK has consistently strong microbial science and synthetic biology research capabilities across the country, particularly in leading institutes such as Nottingham, Oxford, Cambridge, Imperial College and Edinburgh. This means the UK would be exceptionally well-placed to make meaningful progress on the following areas:

#### Suppressing hyper-branching of filamentous fungi

Prolonging continuous cultivation of filamentous fungi by suppressing hyper-branching could improve texture and boost production efficiency.

#### • <u>Comprehensive microbial screening to identify new protein</u> production candidate strains

A systematic, open-access, comprehensive analysis of novel microbial strains could drastically expand the available strains that can compete on flavour, efficiency, cost, and nutrition.

#### <u>Microbial strain-development contract research organisations for</u> <u>fermentation applications</u>

It may be more efficacious for startups to optimise strain productivity by engaging contract research organisations with both deep microbial strain development expertise and also intimate familiarity with the unique considerations of the fermentation sector.

#### Biosynthetic pathway discovery for fermentation-produced molecules

Microbial biosynthetic pathways have not yet systematically been mined computationally to identify candidate pathways for manufacturing high-value ingredients via fermentation.

- **Expanding options for food-safe genetic selection markers** The sustainable protein field would benefit greatly from an analysis of which food-safe selection markers exist and can be used orthogonally, as well as efforts to develop new selection markers.
- **Producing animal-like fats through microbial fermentation** Microbial fermentation may be able to help us produce lipids that are identical or similar to animal fats—especially saturated fats, which are exceedingly rare in the plant kingdom.
- Fat production & encapsulation within oleaginous yeast Oleaginous yeast with durable cell walls may be able to serve as natural methods of fat encapsulation to protect fats through manufacturing, storage, and preparation.
- Novel methods for long-chain omega-3 fatty acid production As the plant-based and cultivated seafood industries scale up, a low-cost and abundant source of long-chain omega-3 polyunsaturated fatty acids will become necessary. Additional innovation is needed to build a robust and scalable supply chain, particularly around precision fermentation and cell-free systems.

## **Cultivated priority areas:**

The UK has particularly high potential to establish leadership in cellular agriculture, due to its combination of expertise in agricultural and veterinary science (for example, centres such as the Roslin Institute and Leeds University), together with its world-beating excellence in stem cell research and biology (for example, The Cambridge Stem Cell Institute, Exeter University, Kings College London, Imperial College and Edinburgh). Some of the priority areas for UK funding include:

#### WHITE SPACES OF PARTICULAR RELEVANCE TO ANIMAL SCIENCE, STEM CELL & CELL BIOLOGY RESEARCH:

#### • Establishment of cell line repositories and standardised isolation protocols

Development of humanely-sourced and thoroughly documented and characterised cell lines from a variety of common food species—together with a mechanism for licensing and distributing these lines to researchers and companies—will remove a key barrier to entry into the field of cultivated meat. In addition, development of open-access, standardised protocols for performing cell isolation from a variety of source tissues and establishing robust cell lines will streamline the processes for those who do end up needing to perform their own isolation and cell line establishment.

#### • <u>Species-specific genomic studies enabling assay development</u> <u>for regulatory standards and cell line optimisation</u>

A suite of assays and genomic knowledge exists for humans and commonly used laboratory species such as mice or fruit flies. However, the same species-specific infrastructure does not exist equally across the species used in cultivated meat, with an especially large gap in seafood species. Commercialised, • <u>Understand animal and cellular efficiency, yield, and input</u> Because cultivated meat replicates the fundamental biology of the source animal, animal-level data may be informative for predicting cellular behaviour in culture.

#### Metabolic modelling for cultivated meat

Academic researchers or consortia consisting of several cultivated meat companies should undertake research aimed at understanding metabolic pathways and fluxes within cultivated meat-relevant cell types. The outputs of this research could be used to improve the efficiency of media optimisation efforts and to enhance the organoleptic and nutritional properties of cultivated meat products.

#### • <u>Mapping the secretome of animal myoblasts, adipocytes, and</u> <u>other cells used in cultivated meat</u>

Stem cells secrete a variety of signalling factors that can influence the behaviour of surrounding cells, known as paracrine signals. In high-density bioprocesses, these secreted factors can accumulate to concentrations that can dramatically influence productivity and standardised assays for species identification such as Short Tandem Repeat (STR) or Cytochrome C Oxidase I (COI) assays are needed. Additionally, richer genetic datasets, including thorough genome annotations that facilitate identification of safe harbour loci, can broadly accelerate cell line optimisation studies.

#### Developing assays for meat-specific cell traits

Research to align on the appropriate assays would introduce standardisation that can accelerate R&D efforts.

<u>Guidelines for cultivated meat starter cell selection</u>

Improving our understanding of the relative advantages and disadvantages of different cell types for cultivated meat would enable researchers to make these decisions more effectively with less duplicative effort.

#### • Systematic investigation of growth factor needs and effects

Open-access research into growth factors required for proliferation, maintenance, and differentiation of cell types relevant to cultivated meat will support both academic and industry research efforts. This research could include screening of species-specific growth factors under a variety of conditions and in a variety of cell types to characterise cross-species compatibility. Research should also seek to define optimal concentrations of individual growth factors and cocktails for achieving various cell states or behaviours, as well as understanding interactions between growth factors. behaviour of neighbouring cells. By mapping the secretome of animal myoblasts, adipocytes, and other stem cells used for cultivated meat, a better understanding of which factors influence proliferation, differentiation, and other cellular traits can be obtained. Mapping efforts will inform how to best leverage this knowledge to improve cultivated meat production.

#### Open-access formulations & optimisation methods for cell culture media and growth factor cocktails

The availability of more open-access formulations will provide a foundation to enable both academic researchers and startup companies to develop their own customised formulations with far less effort and cost.

#### Fat uptake & biosynthesis in cultivated meat cells

Determining which lipids muscle and fat cells are capable of producing and absorbing directly from cell culture media.

#### Incorporating omega-3s into cultivated seafood

Cultivated seafood will need to be supplemented with long-chain omega-3 polyunsaturated fatty acids to be nutritionally equivalent or superior to conventional seafood. However, how these compounds can best be incorporated has not been determined, and there are several potentially-viable strategies. Further research is needed to determine which strategies are most cost-effective and scalable and whether there are appreciable differences between methods in the quality of the final product.

#### Growth factors from conditioned cell culture media

Rather than relying on recombinant growth factors, cultivated meat companies could use conditioned media from animal cells producing high levels of these molecules.

Species-specific research toolkits for cultivated meat-relevant
 species

Coordinated efforts to develop standardised, comprehensive research toolkits of meat-relevant species would exponentially accelerate cultivated meat research.

#### • <u>Understanding uptake and interconversion of omega-3 fatty</u> <u>acids by cultivated fish cells</u>

Although fish are one of the best dietary sources of long-chain omega-3 fatty acids (FAs), these compounds are mostly bioaccumulated from a fish's diet rather than synthesised de novo. Consistent with this, studies have found evidence of reduced omega-3 content in fish as a result of replacing fish-based feed with plant-based feed. Therefore, for cultivated fish to compete with conventionally-produced products, it will be necessary to identify cost-effective strategies for increasing the content of nutritionally-important omega-3 FAs in cultivated fish.

#### WHITE SPACES OF PARTICULAR RELEVANCE TO TISSUE ENGINEERING AND REGENERATIVE MEDICINE:

#### <u>Computational models of perfusion flow through scaffolds</u>

For tissue-structured cultivated meat production, the transition from the proliferation phase to differentiation phase may involve seeding cells onto a prefabricated scaffold within a perfusion bioreactor. Medium is then perfused through the cell-laden scaffold, providing nutrients and oxygen as cells differentiate and mature. Computational models are needed to describe fluid flow through scaffolds to better understand mass transfer and shear forces. These models will inform considerations for scaffold materials, geometries, dimensions, fabrication methods, and bioprocess design as well as considerations for the composition and viscosity of the medium.

#### • <u>Scaffolding development for culinary and biomechanical</u> requirements of cultivated seafood

A number of published studies have focused on scaffolds for cultivated meat (see Related Efforts) yet, to our knowledge, no studies have specifically attempted to formulate scaffolds for fish or tested growth of fish cells on scaffolds developed for terrestrial meat. Because fish uniquely differ from terrestrial meat in structure, research aimed specifically at developing and testing scaffolds for fish products would advance the industry. Both scaffolding materials as well as methods for achieving the correct three-dimensional structure should be investigated.

#### <u>Improving affordability, nutrition, and organoleptic properties</u> of cultivated meat through co-cultures with support cells

Cultivated meat research focuses primarily on muscle fibres and fat cells. However, the other cell types in muscle serve important functions that are potentially underappreciated in their relevance to cultivated meat. In the context of a whole animal, muscle tissue does not exist in isolation. Research into co-culture methods with various support cells could solve a variety of challenges on the road to developing affordable, high-quality cultivated meat.

#### Biomaterials for scaffolding

A handful of companies and researchers are developing scaffold materials for use in various steps of the cultivated meat production process, but to date the topic of scaffolding has been largely overshadowed by the challenge of producing cell mass at scale. This topic needs much more R&D as the industry matures in order to enable the development of products that have meat-like structure and texture, which will be more appealing to consumers than unstructured meat products.

#### Semi-continuous bioprocess for whole cut cultivated meat using simultaneous perfusion and stretch

Stretching of engineered muscle constructs has been previously demonstrated to induce alignment and maturation of muscle fibres, which is desirable for whole cut cultivated meat. Stretch stimuli could also be incorporated into a semi-continuous bioprocess in which a piece of tissue is expanded over time and portions of the tissue periodically harvested. The large amount of meat produced could offset the high initial cost of fabricating a construct capable of continuous growth.

#### • <u>3D microenvironments for cell expansion</u>

Proliferation and high-density cell growth are fundamentally important to scaling cultivated meat production. Recent demonstrations of stem cell expansion in 3D microenvironments such as encapsulated spheres or tubules can generate cell densities far higher than industry-leading stirred tank bioreactors with minimal loss of cell viability or stemness. As a scalable platform, the use of 3D microenvironments for stem cell expansion and differentiation—particularly with the relevant cell types used in cultivated meat—warrants further investigation.

#### • <u>Improving efficiency and assessment of adaptation to</u> <u>suspension growth</u>

Improving methods for adapting cells to suspension culture can facilitate cell line development and bioprocess design for cultivated meat.

## Plant-based, fermentation and cultivated production processing priority areas:

Finally, the UK is also home to expertise in the areas of food science and formulation - with institutes of excellence including Greenwich, Nottingham, Glasgow, King's College and Kent. The UK could therefore play a significant role in addressing the following white spaces:

#### Production process innovations for fibre formation and improved plant protein texturization

High moisture extrusion is currently the most widely used technique for plant-based protein texturization, but innovative alternatives to extrusion are desperately needed. Fibres from techniques like electrospinning, jet spinning, or blow spinning may be able to impart texture throughout a product even if they do not comprise the bulk of the end product, which may render these approaches economically viable for enhancing texture within a bulk product even at a relatively small scale..

#### • <u>Preventing oxidation of omega-3 fatty acids before and after</u> addition to plant-based and cultivated seafood products

Deeper fundamental knowledge of the causes and prevention of oxidation of omega-3 fatty acids before, during, and after addition to plant-based and cultivated seafood products is needed to improve their nutritional and organoleptic properties. There is a need for antioxidation methods to be tailored to the formulations and processing of plant-based and cultivated seafood products, or perhaps new methods must be developed altogether.

#### Plant-based ingredient analytical and characterisation service

Plant-based food manufacturers often struggle with batch-to-batch ingredient inconsistency and variability between suppliers. Better analytical tools for predicting plant-based ingredient performance could improve manufacturing efficiency and create more transparent ingredient markets.

# Fat and moisture encapsulation techniques for sustainable protein applications

Plant-based, fermentation-derived, and cultivated products will all require solutions for encapsulating fat and moisture to ensure that these components are protected from damage or loss throughout manufacturing, storage, and preparation.

#### • Expanded product development in plant-based meat snacks

Plant-based meat snacks could tap into underlying trends in snacks replacing meals and increased consumer interest in high-protein, low-sugar foods. Product innovation is needed to match the taste, price, and availability of animal options.

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