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1	How to eat an idea – a roadmap for the tran	nslation and impact in plant biology
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- 10 Introduction
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As we approach the end of the first quarter of the 21<sup>st</sup> century, it seems as if there has never been a better 12 13 or more exciting time to work in the field of biological research. New tools such as CRISPR-Cas genome 14 editing combined with cheap and accurate genome sequencing are helping us to unravel genetic complexities at previously only dreamt of rates. Advances in mass spectrometry and metabolomics allow 15 16 for accurate identification of chemical compounds previously undetected. In addition, the power of first machine learning and now artificial intelligence (ubiquitously referred to as AI) enables previously 17 incomprehensible volumes of data to be sorted and mined – the most visible example being the AlphaFold 18 programmes which can predict (with high accuracy) the structure of any protein sequence deposited in 19 20 the databases. Compared with the technologies that were in-play only 30 years ago, science seems to 21 have undergone a quantum advance in terms of the tools that are widely available to the global cohort of 22 researchers. Equally, that community is now better connected, socially and professionally, with instant 23 access to data and publications in a fashion that bears no resemblance to the analogue and hard-copy 24 world that those of us who started our careers in the 20<sup>th</sup> century experienced.

But simultaneously, there has probably never been a more challenging time for humankind and all the species that inhabit the planet Earth. This is predominantly driven by the currently inexorable changes in climate as a consequence of human activities such as fossil-fuel combustion and parallel actions such as massive deforestation, exploitation of non-renewable natural resources and pollution of the environment. Changes in the environment also drive alterations in our ability to grow and protect the crops that we rely

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on to feed 8 billion people, as well as exposing us to new diseases as vectors adapt and exploit altered
 climates (Pesaresi et al., 2025).

3 The recent Covid19 pandemic demonstrated that science and innovation can, when both the need and 4 focus are intense, provide technological fixes to resolve a major crisis; in that case with the very rapid 5 generation of vaccines and the perhaps greater logistical challenge of scale-up to meet global demands. 6 Although Covid 19 was a very specific crisis, many different strands of research (academic, industry) from 7 across the globe combined in an unprecedented fashion to generate the tools (diagnostic kits, vaccines, 8 therapies) to allow societies to return, in the main, to normality. Such concerted and collaborative efforts 9 should represent a paradigm for addressing the even greater challenges (climate change, food security 10 etc) we now collectively face.

11 With that in mind, this article will consider how the field of plant biotechnology can contribute to 12 responding to these challenges, specifically in terms of delivering real-world solutions – by that I mean an 13 actual, tangible product or practice that adds (hopefully improves) to our existence and that of the planet.

14

15 Partly as a reflection of the above-mentioned golden period in the advancement of technologies, 16 academic research in the life sciences has boomed in the last few decades, including in research on plants 17 and crops. Botany, a subject that was once considered something of an academic backwater, is now rightly 18 recognised as fundamental to life on Earth. Without photosynthetic plants and algae, our planetary 19 atmosphere would be radically different and unlikely to support life as we know it. Moreover, the same 20 process of fixing carbon generates the staple foodstuffs on which the global population depends for 21 nutrition. Given that the Plant Kingdom plays such a pivotal role in the continued existence of Life on 22 Earth, it is also important to recognise that (like many natural resources) it is not a something we should 23 look to dominate – rather, we should aim to co-exist with in a harmonious fashion. The challenge is how 24 to achieve this without compromising food security for a growing global population, with this requirement 25 and the associated paradigm defined as 'sustainable intensification' (Baulcombe et al., 2009). In a more 26 detailed extension of considering how to ensure not just sufficient calories but optimal nutrition for all 8+ 27 billion mouths, Willett et al (2019) proposed the Planetary Health Diet, integrating food production within 28 the constraints of so-called Planetary Boundaries (PBs). These PBs represent both natural capital and input 29 resources, and whilst the scenarios modelled by the authors continuously evolve, this study ("Food in the 30 Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems") should be

required reading for all scientists active in the Life Sciences, especially those of us who are focussed on
 combining discovery research with translational, applied outcomes.

3 So given that there is an urgent need to provide practical, real-world solutions to some of the many 4 challenges facing the planet, it seems appropriate to provide a simple guide as to how to move a project 5 from a research phase into what can be considered a 'development' phase. Most likely, in previous times, 6 the latter would have been defined as applied research and as such, considered less important than 7 fundamental research (which of course was the literal precursor). Fortunately, we live in slightly more 8 enlightened times, and the need for translational activities is well-recognised and appreciated. Moreover, 9 a burgeoning entrepreneurial subculture is now equally well established as part of the research ecosystem 10 and a key component of the knowledge-based bioeconomy. Thus, start-up and spinout ventures are now 11 common occurrences, and in the area of plant sciences considered here, already starting to have tangible 12 impact (which is here defined as economic and/or societal benefits). This is a significant positive 13 diversification in how outcomes are delivered since previously the primary (if not sole) pathway was via 14 large multinational companies, although they should be better appreciated for their key role in developing the traits that are currently deployed at scale (Napier et al., 2019a). Equally, efforts from the public sector 15 16 have been successful a delivering useful and impactful innovations, in the form of GM papaya that was 17 resistant to papaya ringspot virus (Tripathi et al., 2007).

### 18 Every End has a Beginning

19 So, how do you start? First, one obviously needs a discovery that warrants further evaluation and 20 development towards a prototype (or minimum viable product in business-speak), and as an example, I 21 will use the experience gained and observed from converging efforts by multiple research teams to 22 engineer transgenic plants with the non-native capacity to synthesis omega-3 long chain polyunsaturated 23 fatty acids (colloquially known as omega-3 fish oils) (Napier et al., 2020; Mackintosh et al., 2023). These 24 omega-3 oils have proven human health-beneficial properties and are key ingredients in many animal 25 feeds (including aquafeed) but represent a diminishing natural resource (Tocher et al., 2019). For this 26 reason, quite early in the development of GM oilseed crops, this trait became an obvious (economic, 27 societal, environmental) target. However, unlike the GM input traits (herbicide tolerance, insect resistant) 28 that were rapidly developed and commercialised in 1990s, so-called output traits have been much slower 29 to advance to the same point, predominantly because they are significantly more complex in nature 30 (Napier et al., 2019). For example, herbicide tolerance can be conferred by a single gene, whereas traits 31 such as omega-3 LC-PUFAs require at least five genes. Initial attempts to assemble the biosynthetic

1 pathway in model systems (yeast, Arabidopsis) confirmed the functionality of the heterologous genes 2 encoding the enzymatic activities (desaturases, elongases) and allowed for a more targeted phase of 3 activities focussed on demonstrating that these transgenes could be co-ordinately expressed in a tissue-4 specific (seed) manner, altering the seed fatty acid composition and importantly observing that these non-5 native fatty acids were accumulated in the storage lipid (triacylglycerols) of the seed (Venegas Caleron 6 and Napier, 2023). From a metabolic engineering perspective, optimising this process is fraught with 7 jeopardy, since although the heterologous omega-3 pathway is being generated by the action of at least 8 5 transgenes, for the pathway to be active requires the simultaneous contribution of multiple endogenous 9 components too (such as electron transport chain partners, acyltransferases, reductant generation etc). 10 It is for this reason that this particular engineering has been likened to the trans-dominant metabolic reprogramming observed in some marine viruses (Michaelson et al., 2010). Equally, although 11 12 contemporary thinking often portrays transgenesis and dependent disciplines (including Engineering 13 Biology) as highly predictive and precise, this is more an aspiration than fact. In reality, plant genetic 14 engineering still continues to teach us how little we understand the systems we are trying to manipulate 15 (Dong and Ronald, 2021).

16 Having achieved what can be considered a proof-of-principal (PoP) (in this case, that transgenic plants can 17 synthesise and accumulate the omega-3 fish oils EPA and DHA in their seed oils), efforts were then focussed on demonstrating Proof-of-Concept (PoC), i.e. that this innovation could stably work in the real 18 19 world and at scale (Khaipho-Burch et al., 2023). In research using plants as the host, it is often assumed within the academic community (but much less frequently demonstrated) that any new discovery will be 20 21 compatible with the pre-existing agricultural systems and can be simply adopted in a plug-and-play 22 fashion, irrespective of the background germplasm. Sadly, this is wishful thinking and only emphasises the 23 gap between fundamental plant sciences research and translational efforts using agriculture – collectively, 24 we must strive to close this gap. Perhaps the first (and critical) step on the PoC journey is to carry out field 25 trials to confirm the stability of the novel (GM) trait and also the ability of the modified plant to withstand 26 the gauntlet of the variability and stresses of the natural environment. It is a seductive fallacy (enabled by 27 experimental designs with a dependency on highly controlled environments) that results obtained in CE 28 cabinets or glasshouses will be directly replicated in field conditions (Nelissen et al., 2020). Unfortunately, 29 this is rarely the case (if at all), although logically it is equally unsurprising – no field has a stable 30 temperature, month after month, with sunset and sunrise at exactly the same time each day, yet this is 31 the paradigm that underpins much of fundamental plant sciences today (Fig.1). So, it should not be a 32 shock that many discoveries that showed promise in contained environments fail when they come face1 to-face with cold (or hot) hard reality (Inze & Nelissen, 2022; Nelissen et al., 2020). As a first step, we as 2 a community need to very quickly incorporate field evaluation into the DBTL (Design-Build-Test-Learn) 3 rationales for plant Engineering Biology, at least for any target traits that is envisaged to be deployed at 4 scale – this should be also costed into funding bids, to enable such work and also as a clear sign of intent 5 to funders. Given that one of the strongest arguments for using a plant chassis in Engineering Biology is 6 that you can harness the pre-existing know-how and infrastructure of agriculture to deliver massive 7 volumes of product that would be prohibitive for any fermentation-centric chassis, it is genuinely 8 surprising that field evaluation has not yet become a central component of plant Eng Bio DBTL, unless 9 counterintuitively, all the traits under development are not required at scale.

10 Although the field is the obvious destination for a plant-based innovation with potential, there are a 11 number of real or perceived barriers to achieving this stage. Firstly, it might be that the innovation/proof-12 of-principle has been constructed in a plant species that it not suitable for field evaluation. This is less 13 common now that much research is carried out directly in crops as opposed to model systems, but a 14 significant volume of discovery research is carried out in Arabidopsis thaliana. Other established or emerging Engineering Biology model systems such as Physcomitrella patens, Marchantia polymorpha and 15 16 Brachypodium distachyon have undergone limited to negligible evaluation in native conditions, and whilst 17 some commendable efforts were made in the past to establish protocols for transgenic Arabidopsis field 18 trials (Frenkel et al 2008), and also highlighting the importance of field studies for understanding gene-19 environment interaction, such approaches gained little traction at that time with the very large Arabidopsis research community. In the past decade, in a move stimulated by funders and desire to more 20 21 quickly realise impact from fundamental activities, much more research is now carried out directly in crop 22 species, including commodity crops such as wheat, rice, canola and soybean, as well as more niche 23 "boutique" crops such as camelina, pennycress and many others. In theory, once an innovation has 24 reached the PoP threshold in a crop, then it should be straightforward to evaluate performance in the 25 field, either for both general fitness and the specific trait of interest. Disappointingly, the number of field 26 trials of transgenic (GM) plants remains remarkable low, when set against the many hundreds if not 27 thousands of labs generating transgenic plants. To be fair, it is often argued that most research projects 28 are of a relatively modest duration (3-4 years) which might restrict the likelihood of being ready to move 29 to the field. But equally, it is to be hoped that some of such projects are successful in securing a second 30 tranche of funding to advance their research, and since this is likely because of initial success, would it not 31 then be logical to carry out field trials? That this absence of field evaluation serves as a bottleneck for 32 translation and technology transfer is undeniable and also represents an impediment to economic return

1 on the initial investment that funded the research. Irrespective of whether this funding comes from 2 private or public sectors, PoC validation by field testing is currently a missing link for many national 3 programmes, compounded by variations in the ease with which approval to carry out GM field trials might 4 be obtained. For example, approval for environmental release in North America is straightforward and 5 therefore more commonplace than in UK, where the process also involves a 48-day open consultation in 6 which members of the public (actually usually anti-technology NGOs) can make representations to the 7 Ministry responsible for approving such releases. Whilst it is likely that this additional scrutiny can serve 8 as an ideological impediment for some researchers and/or institutions, it can also serve a useful purpose 9 to enhance the clarity of thinking (such as the perceived benefits) associated with a project.

However, in some parts of the world, most notably within parts of the European Union, there is 10 11 strong resistance to even small-scale experimental field trials and researchers in Italy have recently had 12 GM trials vandalised and destroyed (Meldolesi, 2024). Having been witness to the vandalization of GM 13 field trials at Rothamsted in the late 1990s and also seen at first-hand how disturbing the threat of 14 destruction can be (when our GM wheat trial in 2012 was the subject of a campaign to be 'decontaminated' (Nature editorial, 2012), such behaviours are not conducive to a productive research 15 16 culture nor a respectful debate about the pros and cons of technology. Irrespective of these impediments, 17 it is vital for meaningful translation of any biotech innovation to undergo field trials, so mechanisms and 18 processes need to be sought to allow scientific methods to be applied without the risk of sabotage or 19 destruction. In the case of our GM wheat trial, the plants were engineered to constitutively synthesise the 20 sesquiterpene (E)- $\beta$ -farnesene, a volatile compound which is also an alarm pheromone for cereal aphids, 21 which in turn damage plants and serve as vectors for a number of viruses. Lab-based studies identified 22 transgenic wheat lines that emitted (E)- $\beta$ -farnesene capable of repelling colonising aphids as well as 23 recruiting predatory parasitic wasps which use the alarm pheromone as a location cue (Bruce et al., 2015). 24 Equally, using experiments carried out in growth chambers to mimic predicted field conditions confirmed 25 these multitrophic interactions mediated by the transgene-encoded aphid alarm pheromone. However, 26 GM field trials over two years revealed no statistical difference between the transgenic wheat and the 27 controls, in terms aphid repellence or parasitoid recruitment (Bruce et al., 2015). Although an associated 28 commentary described the experiment as a 'failure' (Cressey, 2015), this was not a true representation of 29 the outcome – rather, (and as noted in the same piece) it was a hypothesis there to be tested, and better 30 to know the shortcomings of the current iteration quickly, so that a new one can be developed (described 31 in Cressey [2015] as "try, try again" but equally it could now be described as DBTL). John Pickett, the PI of 32 the Rothamsted project was quoted at the time as saying, "the field is the ultimate arbiter" (Cressey,

1 2015), although it is slightly chastening that this rather obvious truism has, ten years later, still failed to 2 gain much traction within the plant Engineering Biology community (Khaipho-Burch et al., 2023). 3 However, it is equally clear that the combination of concerns over vandalism combined with ingrained 4 aversion to risk (fear of failing) has likely impeded the translation of many discoveries. Perhaps we need 5 to remember that nullifying the hypothesis is not 'failure', simply the scientific method in action. The 6 reality of this is nicely documented by Simmons et al (2019), who report a 1% success rate for the field 7 evaluation of candidate genes in maize.

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9 So, if we are willing to accept the proposition that the "the field is the ultimate arbiter" of the utility of a 10 particular trait or enhancement, how can we fast-track the necessary field evaluation, especially in regions 11 where such trials are contentious? One creative scenario has been developed in Switzerland, in the canton of Zurich, with the establishment of the so-called "Protected Site", a dedicated field-testing 12 13 capability which is available for all researchers to test their GM and GE crops in an area that is secure from 14 intrusion or sabotage. This has allowed Swiss researchers to evaluate their technologies faster than their 15 neighbours in France or Germany, that lack such a capability but also have strong restrictions on GM field 16 trials. In a time when science is considered to operate without borders, it is perhaps pragmatic to consider 17 the utility of field trials in any suitable location, if it allows for initial validation of a PoP. Ultimately, creative solutions need to be found to advance exciting basic discoveries, and these must include the expansion 18 19 of the DBTL process to encompass real-world performance. As a simple demonstration of the feasibility 20 of carrying out cross-border field trials, we at Rothamsted have hosted GE camelina field trials for 21 colleagues in France (Faure & Napier, 2018) and equally carried out GM camelina trials in both Canada 22 and USA (Han et al., 2020). So even if you are based in a location or territory that is not enabling for the 23 field release of GM plants, this need not represent an impenetrable obstacle, rather just an opportunity 24 to look for solutions on a wider horizon. Equally, any hesitancy that is based on a 'fear of failure' should 25 be assuaged by the realisation that iteration and the DBTL cycle is dependent on identifying bugs and 26 glitches (or even system failures), otherwise there is no need for a recursive process. In general, one 27 should always be scanning the horizon for collaborators who have key skills or capabilities to help advance 28 a project. And an informal network of challenge-led, application-driven plant biotechnologists could be 29 an additional mechanism to inject resilience into your innovation journey.

# Although making bold claims about the utility of discovery research is now an engrained and almost

### 1 The Road Less Travelled – the Path to a Product.

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3 mandatory component of securing funding, in reality this is poorly matched by delivery – perhaps 4 fortuitously, there is no official mechanism by which over-claiming is called to account. And although some 5 of this can be excused as over-enthusiasm or perhaps stretch-objectives, equally some of it represents 6 either unfamiliarity with downstream requirements or just plain hubris. Perhaps a useful default position 7 to take is "Don't believe the hype" and more importantly, don't indulge in it either. Although not 8 restricted to plant sciences, there is a simplistic and seductive narrative that we are "feeding the world", 9 which can then play well with funders and also dissemination into the wider media. I would argue that we (as a community) should be much more active in terms of self-policing ourselves in using such rhetoric, as 10 11 repetition (in the absence of real step-change differences) just results in narrative fatigue and a 12 generalised jaundiced view of research. In addition, there is a lack of familiarity within the academic 13 research community as to the multiple steps that are required to convert a validated PoC into something 14 that people might ultimately eat and growers would embrace (Simmons et al., 2019). Some of that might be due to the massive expansion of lab-based molecular studies with a concomitant shrinkage in field-15 16 based studies - here in the UK, many universities no longer have Agricultural Sciences departments or 17 similar, so there is both a lack of experience and an absence of training opportunities. In general, there is 18 a worrying void in knowledge and competencies in how a PoC discovery would be bulked up, deregulated, 19 approved and commercialised. And even if the expectation is that academic discoveries are ultimately 20 brought to market via a public-private partnership (i.e. in collaboration with industry), how will that be 21 achieved? Private industry is driven by the understandable need to turn a profit and answer to their 22 shareholders and investors, and such cold logic is often a rude awakening to academics who are not 23 normally exposed to the brutality of the market – ultimately, if a potential product is not economically 24 viable and stable as an inherited trait, then it doesn't matter how impressive the underlying science is. 25 This is a reality that many in academia find hard to accept, and partly it then drives the "grade inflation" 26 of the overclaiming mentioned above. But we as academics need to better understand the needs and 27 drivers of private industry – it can be highly instructive to spend even a short period of time in that 28 environment, to better appreciate the commonalities and differences between the two sectors. In 29 addition, there are other ways in which useful innovations can reach their targets (Ronald, 2014).

30 When we at Rothamsted initially realised that we had successfully developed a prototype camelina plant 31 that was accumulating commercially relevant levels of omega-3 long chain polyunsaturated fatty acids,

1 the project was greatly enabled by two fortuitous factors. Firstly, the senior leadership at the time had 2 significant experience in developing biotech traits for translation beyond academia and were familiar with 3 the regulatory approval processes in different regions and countries (Nelissen et al., 2014). There was also 4 a strong realisation that to maximise the credibility of our prototype, not only did it have to be based on 5 solid biological data (e.g. multiple independent transgenic events, validated by field trials), but the basis 6 of the economic opportunity also needed to be quantified in detail and sense-checked at every step 7 (Clarke and Zhang, 2013). The importance and power of this approach has recently been highlighted by 8 Oliveira-Filho et al (2024), who very nicely articulate the value of these Fermi calculations in substantiating 9 (or not) the plausibility of a particular approach. One key step forward in progressing our technology was 10 to appoint a business development expert, with the appropriate skills in financial analysis and commercial planning. Such skills are obviously different from those of a plant biotechnologist (such as this author), 11 12 but they represent key competencies that will be required in the transition from academic research 13 through to development and ultimate commercialisation (Barnes, 2025). Equally important, it is critical to 14 have a clear understanding of the regulatory requirements for bringing a GM crop to market - this is a complex process and varies from country to country, and without such approvals it will not be possible to 15 16 commercialise the technology. The approval process is unfamiliar to many but usually is required for 17 cultivation (i.e. growing the novel crop) and (separately) for use as a feed or food. It can be daunting to 18 navigate the requirements for these approval processes, and perhaps more challenging are the costs 19 associated with generating the data packages that are required by the national agencies that provide 20 regulatory approval (the mechanism by which the safety of a new innovation is determined). For example, 21 approval in the US for the commercial cultivation (referred to as deregulation, as a successful approval 22 removes the GM event from regulated oversight) will require several years' worth of multilocation field 23 trials, in addition to genomic and proteomic confirmation of the trait stability (Napier et al., 2019b; 24 MacIntosh et al., 2023). Although the former is now significantly more straightforward, accurate 25 quantitation of transgene-encoded proteins remains technically challenging (Bushey et al., 2015). 26 Collectively, obtaining the information required for regulatory approval will likely cost several million 27 dollars, as well as taking significant time (including that required for additional field trials), and is usually 28 restricted to an actively selected lead event. Unfortunately, this process is very often not fundable via the 29 predominant public sector mechanisms which support the (precursor) discovery research - in other 30 words, there is an apparent disconnect where research is advanced to a particular technology readiness 31 level (TRL) but then ineligible for further to support which might facilitate the final phase of translation 32 and commercialisation. One likely reason for this is the (logical) expectation that innovations developed

1 in the public sector (academia) will likely need to be brought to market as a public-private partnership i.e. 2 with private industry providing know-how and expertise on the commercial side of things (Ronald, 2014; 3 Simmons et al., 2019). However, it could be argued that this model is slightly old-fashioned and doesn't 4 fully reflect the more entrepreneurial ecosystems that now exist on many university campuses and 5 research parks. Instead, there is a need for access to experts who can provide a pragmatic analysis of what 6 is needed to ensure regulatory approval, without this being a component of a wider business relationship 7 - in other words, bespoke consultancy-based regulatory analysis which in turn then allows the creators 8 to obtain additional funding (from venture capitalists, investors, etc) because they can correctly define 9 the costs that need to be expended to obtain deregulation. And assuming that these costs can ultimately 10 be covered by revenue and profit from the sale of the final product - information that will have been 11 generated by the business development expert as part of their market opportunity and business case – 12 then it will be significantly easier to convince investors and raise the necessary funding for regulatory 13 approval.

14 In my experience, we tend to consider many of the post-PoC activities we have undertaken as 'derisking' - not for our technology per se, but rather to reduce the apparent risk to investors and stakeholders. For 15 16 example, our technology (GM camelina plants engineered to make omega - 3 fish oils) has a primary market 17 opportunity in servicing the needs of the aquaculture industry (Napier et al., 2020), which currently uses 18 unsustainable marine extraction as a source of fish oils that are essential for marine fish farming (Tocher 19 et al., 2019). To demonstrate that the EPA+DHA rich camelina oils derived from our transgenic plants were 20 suitable for use in aquaculture as a drop-in replacement for oceanic-derived fish oils, we carried out 21 multiple fish feeding studies and confirmed the utility of our novel oil. Importantly, the camelina oil was 22 shown to be safe and efficient as a feed ingredient for multiple different commercial fish species (Tocher 23 et al., 2024). Although such studies are unlikely to be published in the more prestigious journals usually 24 associated with academic success, they demonstrated successful translation of our technology and the 25 associated derisking. Quite rightly, investors need to be reassured that any money they invest in a 26 technology that is not going to fail at an early stage of the development cycle, since they expect a return 27 on their investment. In the case of our aquafeed trials, until we tested the suitability of our oil as a 28 component of the diets, we were dealing with an unknown. And whilst one would logically predict that 29 our GM-derived oil would be functionally identical to an oil derived from marine extraction, until this is 30 experimentally proven it represents a risk and potential barrier to investment. It is for this reason that we 31 have subsequently demonstrated that utility of our oil as a component of diets for salmon, trout, sea bass, and tuna, since each represents another "unknown". But another benefit of these studies is that they 32

represented an opportunity to bid for research funding for support that was distinct from the preceding grants. One significant challenge facing public sector funded research can be characterised as the 'cult of novelty', where funding agencies and journals are enthralled to the concept that novelty is a justification in itself. But just because something is novel doesn't mean it has an intrinsic worth (academic or otherwise). Ultimately, there is a balance to be struck between advancing the project whilst satisfying the needs of the funding agency, but sometimes it can be useful to restate that translation can be novel too.

### 7 Intellectual Property – the patented elephant in the room

8 One additional consideration in any plans for the translation and commercialisation must include 9 intellectual property and patents. Although perhaps underappreciated, the patent mechanism provides a 10 means by which an invention is protected and rewarded. In the case of publicly funded research, patents 11 provide a key route for recovering the investments made by the taxpayer. Amongst academics, there is 12 also a suspicion that patents prevent innovation, but that is likely based on a lack of familiarity with 13 intellectual property rights and that in general, patents actually foster innovation. One key action in 14 planning the commercialisation of a validated prototype should be to carry out detailed analysis of the 15 patent landscape around this technology – this should also include so-called freedom-to-operate (FTO) 16 analysis, which determines if your invention is encumbered by any other IP, along with the more 17 straightforward determination of whether or not your discovery is novel and patentable. Although such analysis is often undertaken by specialists (patent attorneys), it is possible for the academic researcher to 18 19 carry out much of this analyses themselves, using excellent search tools such as The Lens (www.lens.org) developed by Cambia (established by Richard Jefferson, a plant biotechnologist best known for 20 21 popularising the GUS reporter system in plants). Tools such as The Lens were specifically developed to 22 empower and enable researchers to better understand IP networks and to have greater control over their 23 inventions, and in that respect, I would strongly encourage all researchers to use them to investigate the 24 IP surrounding their gene of interest. Often, academic researchers are surprised (and slightly horrified) to 25 discover that "their" gene has already been the subject of a patent, but this knowledge can be 26 empowering, since it helps to crystalise an understanding of wider interest in any given technology and 27 also provides an opportunity for transactions and business development. Perhaps surprisingly, the total 28 patent literature is enormous, a dominant "dark matter" that the vast majority of academic researchers 29 ignore or are oblivious of. But I would again encourage everyone to investigate the patent literature, 30 because you will discover that it contains many advances and innovations not reported in the conventional 31 scientific literature. Routinely searching the patent databases is obviously an absolute requirement for

successful commercialisation of a technology, but in general, it should be an activity that is included in
 general good practise for conducting research, otherwise any familiarity with the state -of-the-art will be
 partial and incomplete.

4 It is also worth emphasising that just because something is already patented, this doesn't preclude others 5 working on it or aiming to improve the invention. In fact, it is often possible to obtain new IP based on 6 making an improvement to a system. Equally, the presence of a patent should not be seen as a block or 7 impediment to others using the patented technology - probably the best current example of this is 8 CRISPR-Cas9-this technology is subject to complex IP claims and grants but is also now a universally used 9 research tool. This also serves to emphasise the possibility of using patented inventions for research purposes (so-called research use exemptions), although these vary from region to region and are usually 10 11 restricted to specific academic endeavours. In the case of the CRISPR IP, the patent owners have granted 12 research exemptions, allowing this powerful technology to be used freely in academic research (e.g. Li et 13 al, 2022). Obviously if the technology is used to develop something useful (i.e. a new 14 invention/prototype), then this would be dependent (encumbered) on the original foundation IP and any commercialisation would likely require a license from the owners of that IP. Some very useful lessons from 15 16 the Golden Rice story are recounted by Dubock (2014) including the importance of understanding IP, even 17 in the context of an innovation with a non-commercial focus.

## 18 Box 1: Some Key Considerations

When considering how to develop a discovery (or even just an idea) into a product, all of the followingshould be given significant attention and thought.

- Have a very clear and precision vision of success what it is that you are trying to create, and how
- Understand the realistic timescales to achieve this success, including the constraints of
   seasonality map these out.
- Analyse and investigate the intellectual property landscapes which will almost certainly pre-exist
   and impact on your idea. Don't be put off by prior art but seek professional advice from qualified
   patent attorneys once you have done your own analysis.
- Understand the market opportunity that you believe underpins the economic case for the
   ultimate commercial success for your invention.
- With the help of a business development professional, develop a business development plan
   which realistically captures costs and potential returns

- Understand the regulatory landscape that covers your technology, covering both initial
   translation (e.g. research GM field trials) and full commercial regulatory approval. This will likely
   also require specialist input from experts. Appreciate the data packages that are required for such
   approvals and the associated requirements in terms of time and money.
- Build a network of colleagues that share your vision and ambition. This should extend beyond the
   research environment and be more than an echo-chamber. This can help sense-check a direction
   of travel or trouble-shot a roadblock.
- Adopt an entrepreneurial mindset and relish the challenges this journey will certainly bring. Don't
   see knockbacks as failures, but opportunities to learn.
- Keep the faith in your idea if you don't believe in it, why should anyone else?
- 11

### 12 Conclusions

13 Bringing an innovation to market is very far from the normal academic experience but it represents the 14 opportunity to deliver real-world impact (and all the benefit that might bring) as well as deliver personal 15 growth. It is for good reason that I have often described this journey as 'The Road Less Travelled' 16 (borrowing from the same title of a book by M. Scott Peck), since it is not an opportunity that is presented 17 to all, and equally, not a road that everyone is interested in choosing to travel. But equally, and here 18 reflecting the focus of Peck's book, I believe that actively engaging with the challenges associated with 19 converting an idea into a tangible product is both positive and enhancing (professionally and more widely). 20 What I have tried to outline in this short article, with the help of some examples and my own experience, 21 are the steps that need to be taken to advance from the initial excitement of discovering something new 22 and useful, all the way through to bringing a product to market. I am providing this with the benefit of 23 hindsight, and certainly if I had to rerun my omega-3 project again, I would certainly do things differently. 24 But ultimately, we all can only do the best we can, with the cards that we hold at the time. One very 25 positive development in recent years have been to greatly encourage entrepreneurial approaches within 26 academia and I believe that this has also created a more robust and vibrant culture in terms of innovation, 27 translation and impact. It is also very encouraging to see others recently documenting their similar 28 journeys on bringing innovations to market (Martin and Butelli, 2024) Given the many challenges that we 29 all face, this can only be a good thing, and hopefully many more people will get to literally eat our ideas.

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- 1 Figure Legend
- 2 Figure 1.
- 3 Visual comparison of Camelina growing in the field and in a controlled environment. Panel A transgenic
- 4 Camelina plants grown (under Consent 23/R8/01) on the Rothamsted Research experimental farm in
- 5 Summer 2024. Panel B maximum monthly average temperatures recorded at Rothamsted during the
- 6 growing season (2021-2024) dotted lines at temperatures referred to in (C). Panel C similar lines grown
- 7 in CE cabinets at Rothamsted Research; the set temperature is 21°/18°C on a 16/8 day/night cycle. Note
- 8 that this bears little similarity to what the crops experiences in the field.



Maximum temperature (C





В

**Figure 1.** Visual comparison of Camelina growing in the field and in a controlled environment. Panel A – transgenic Camelina plants grown (under Consent 23/R8/01) on the Rothamsted Research experimental farm in Summer 2024. Panel B – maximum monthly average temperatures recorded at Rothamsted during the growing season (2021-2024) – dotted lines at temperatures referred to in (C). Panel C – similar lines grown in CE cabinets at Rothamsted Research; the set temperature is 21°/18°C on a 16/8 day/night cycle. Note that this bears little similarity to what the crops experiences in the field.

Figure 1 339x190 mm (x DPI)