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From Innovation to Application: Bridging the Valley of Death in Industrial Biotechnology

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Few biotechnology innovations make it through the Valley of Death to markets. Based on our experience with academia, technology transfer offices, and industry, we provide insights into differences in operating levels, how to best traverse the Valley of Death, and ways to foster more innovation towards market implementation.

The Rise of Biotechnology

The rise of biotechnology is evident from the increase in global market value to a forecast of US$2-4 trillion by 2030–2040 [1]. A substantial part of the applications of the field relies on microbes, which are applied to produce an ever-larger variety of chemicals and enzymes with industrial value [2–4].

Heavily as industry has grown to depend on microorganisms, only one in 5000–10 000 biotechnology innovations derived from academia survives the long route from the initial findings to product commercialization [5]. Generally referred to as the 'Valley of Death' [6], the division between innovation and application starts at the different product development levels at which academia and industry operate, known as technology readiness levels (TRLs) [7]: typically TRL 1–3 in academia and TRL 8 and 9 in industry. At TRL 4–7, the discovery process is generally considered too applied for further scientific funding but too risky to fund for industrial market implementation. Other reasons why new technology often does not bridge the Valley of Death include cumbersome contracting or procurement of technology requirements, lack of exposure, lack of entrepreneurial management, lack of adequate funding for further development, and lack of a strong link between technology development efforts and industrial deployment [8].

We recently conducted a series of in-depth interviews to gain insight into the perceptions and differences between industry and academia to understand and contribute to narrowing the Valley of Death in industrial biotechnology (Box 1). By interviewing participants from both fields, including companies of different size and from different areas of the world, we were able to get a clear snapshot of the state of affairs [9]. In this article, we highlight the main outcomes of our investigation, pinpoint what causes the difference in operating levels, and make suggestions on how to traverse the Valley of Death.

Different Aims Widen the Valley of Death

Given that academics usually introduce scientific innovations, they often limit their research to proof-of-principle. By contrast, industry needs marketable products, such as titers, rates, and yields, that allow for a competitive business model. Even though this appears rather straightforward, the implications are far-reaching.

Proof-of-Principle and Industrial Process Do Not Match

Academic research fosters novelty and scientific innovation. Its first function is to educate: research is carried out by undergraduate, graduate, and postdoctoral students, who must be allowed to explore, develop, succeed, and fail in their own projects. Research centers and universities need their flexibility for in-depth research, to be able to develop out-of- the-box ideas and ground-breaking discoveries. This results in operating mainly on a small-scale, proof-of-principle, using, for example, expensive feedstocks and highly flexible equipment operating at near-perfect technical levels, all of which are unattainable on an industrial scale. In the long term, this enables the use of exotic microorganisms and the development of novel experimental and computational protocols.

Proof-of-principle is not enough for innovation to gain traction in industry. In addition to the technical considerations and restrictions that academia adheres to, including the type of equipment, familiarity, and ease of working with certain, well-tested microorganisms, industry must consider numerous sector-based and social factors. Production must be cost-effective, sustainable, and safe [10]; thus, industry has adapted microorganisms for a more sustainable production process, increasing the titer, rate, and yield to improve cost-effectiveness. They must follow numerous governmental regulations and ensure a positive public perception of their products. To comply with these strict technical, sector-based, and social regulations while remaining competitive, patents are invaluable.

Introduction of novel microbes is only considered if the production process can remain roughly unchanged, or if the titer, rate, and yield are improved so much that it makes up for the required changes to the production process. As the value of the end-products increases, so does the flexibility of the company.

If a researcher aims for industrial and, thus, market application of their research or invention, such industrial-scale requirements must at least be kept in mind to increase the chances of making it through the Valley of Death.

Box 1. Methodology of the Underpinning Research

In our previous work, we conducted a qualitative and exploratory study comprising a series of in-depth interviews to discover how to improve chances of research surviving the Valley of Death in Biotechnology. Participants were selected based on expertise (professors with and without industrial experience, technology transfer officers, chief executive officers, and chief technical officers), field of research (pharmaceuticals, food, industrial chemicals, or production organism development) and geographical location (Europe or the USA). Four academics, two technology transfer officers, and eight industrial experts were interviewed. During the interviews, the research question of 'Opportunities between industry and academia' was addressed by discussing themes such as common grounds, differences, challenges, possibilities, perspectives, and collaboration between the two. Overlap in answers indicated data saturation, and results were compiled, processed and analyzed [9]. Here, we assess the selected impactful highlights in more detail and use literature to formulate the implications and possible solutions.

Money over Knowledge

Recently, Linton and Xu [6] laid out how appropriate business models are required to prevent failure to qualify or to industrialize new innovations. They indicated that this must be done by reducing resource requirements; avoiding time, cost, and quality trade-offs; and increasing the reward for crossing the Valley.

The duration of scientific research projects and the fast turnover of temporary staff require much funding over a long term with uncertain outcome. Academic groups increasingly depend on earning funding through grants and collaboration projects. Grant applications and collaboration initiatives generally demand an extensive project description, with strictly planned intermediate goals in the form of milestones and deliverables, and a clear application, defined as 'useful in industry and/or society' [11]. However, experts from industry seldomly approach academic institutions, but rather visit conferences and await collaboration proposals to cherry-pick the most applicable and easily adaptable novel research.

As an alternative, collaboration projects are set up between industry and academia. Such collaborations limit publication opportunities: scientific excellence is often measured by publications, whereas industry can only allow publications results concerning TRL 1–3 due to patenting potential, creating a natural stop to research by academics (Box 2).

Size Matters in Innovation

Large companies can stifle the need for academic innovation by setting up their own R&D department. Their size complicates the integration of larger, potentially more impactful innovations. There is no room for high-risk, high-reward solutions. They are limited by their dependence on the existing infrastructure, which again limits their collaboration with academia. Whereas smaller companies generally have fewer funds and must survive a tough competitive environment, they are more flexible and agile and, thus, are able to integrate innovations in their production lines.

Start-Up Companies: Bridge or Break?

Start-up companies are companies that spin off from an academic background to commercialize a promising academic innovation. There is a perception in some sectors that, rather than decrease, start-up companies have in fact contributed to increase the gap between academia and industry: now both must deal with an in-between, and only few entrepreneurial academics have a chance of seeing their invention graduate into an application. This strengthens the cherry-picking abilities of industry even further: larger companies acquire successful spin-off companies, denying their competition access to these innovations.

Nonetheless, the case can be made that start-up companies are a great opportunity to close the gap altogether, easing the transition of academic research to actual industrial application and providing opportunities for academics to focus on education and research [12].

However, despite their potential, start-up companies struggle to live up to it. Smaller companies must survive the Valley of Death by recruiting their own, often limited resources, forcing them to make trade-offs in time, cost, or quality. At the same time, these companies run into the same issues as industry or academia, including those aforementioned such cumbersome contracting or procurement of technology requirements, and lack of exposure, entrepreneurial management, adequate funding, and a strong link between technology development efforts and industrial deployment [12–14].

How to Bridge the Valley of Death

Based on in-depth discussions with experts in both fields, we propose to include innovation-to-application trajectories in all project planning. This would necessitate

Box 2. Other Limitations in Technology Transfer

Although the main focus here is on problems, limitations, and miscommunications occurring during the attempt to traverse the Valley of Death, there are many reasons for academics to not even attempt to bring their innovation to the market. Being driven by the need to teach, conduct research, write papers, and finance their efforts, there is simply no incentive for marketing. Not only does the trajectory cost time and resources better spent elsewhere, but the rewards are also highly limited. Risk of failure is simply too high [6]. In addition, academics must decide themselves which innovations are worth pursuing, and which they think will not make it across the Valley of Death. Communication in these early phases is highly limited: there is a constant pressure in academia to publish or risk their research being scooped.

Although many academic institutions are now providing aid in the form of patenting offices, start-up support, and technology transfer experts [16], a strong incentive is still required to pursue innovation application.

closer communication lines between academia and industry [15]. Including project-specific co-development of research ideas between industry and academia toward clearly marketable goals allows for focused research and decreases the time and resources required for product development. It also requires procurement of the right expertise to handle marketing and business development. This inclusion can be described in the form of start-up companies or lead to including experts from this type of enterprises. As an additional benefit, including a clear business model in any grant application attracts governmental, national, or international funding.

Simply put, we need to include product development preparation before there is a product. To decrease the depth of the Valley of Death, one must start the journey well prepared.

Concluding Remarks

The Valley of Death is a natural distance between two fields with a majorly different aim. Rather than narrowing the gap between academia and industry, we need either preparation for marketable initiatives from the start, or a third party to act as a bridge between the two, both in communication and in the TRL levels.

As such, start-up companies should be naturally included in project planning from start to finish. Their expertise in discovery, scaling-up, marketing, and communication is invaluable in the current process of research and development. Grant applications and collaborations between academia and industry should include some attention for the possibility of start-ups to develop, leading to more attention to industrializing promising results and growing them into market applications from the development stage onwards.

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Declaration of Interests

The authors declare that they have no competing interests.

Authors Contributions

Conceived the study: V.A.P.M.d.S., E.A-G., and L.F.C.K.; literature research: L.F.C.K. and E.A-G.; work supervision: A.W., P.J.S., and V.A.P.M.d.S.; wrote manuscript: L.F.C.K. and E.A-G.; addressed rebuttal: E. A-G., L.F.C.K., and V.A.P.M.d.S.; edited and proofread manuscript: E.A-G., A.W., P.J.S., and V.A.P.M.d.S.; and arranged funding: V.A.P.M.d.S.

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