

# Translating academic discovery to patients' benefit: is academia ready to assume its key role?

Roch Ogier, Wolfgang Knecht, Martin E. Schwab



## **Information on the preparation of the article**

During the retreat of the SAMS Executive Board in September 2016, Martin Schwab, Prof. of Neuroscience at the University of Zurich and ETHZ, reported on current roadblocks in academic translational research. On 2 November 2016, the Executive Board decided to support Prof. Schwab in carrying out a study on the situation of translational research in Switzerland, with the goal of formulating concrete recommendations.

The article «Translating academic discovery to patients' benefit: is academia ready to assume its key role?» is the result of a series of workshops and interviews conducted in Switzerland and abroad in 2017 and 2018 by Roch Ogier, Therapy Development Accelerator, University of Zurich, and Wolfgang Knecht, Zurich Neuroscience Center, University of Zurich and ETHZ, under the supervision of Prof. Schwab. This work was reviewed and commented on by a small working group composed of the following people: Leonardo Scapozza, Swiss Center for Therapeutics Discovery; Werner Enz, Basel Inkubator; Kostas Kaloulis, Catalyze-4Life; Margrit Leuthold, ETHZ; Vincent Wagner, Translation Accelerator; Paolo Pagnetti, Lugano Medtech Center; Martin Kayser, Wyss Zurich; Uyen Huynh-Do, SITEM-INSEL.

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# **Translating academic discovery to patients' benefit: is academia ready to assume its key role?**

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Swiss Academy of Medical Sciences (SAMS)  
House of Academies  
Laupenstrasse 7, CH-3001 Bern  
T + 41 (0)31 306 92 70  
mail@samw.ch  
www.samw.ch

### Authors

Roch Ogier, Therapy Development Accelerator, University of Zurich  
Wolfgang Knecht, Neuroscience Center Zurich, University of Zurich and ETH Zurich  
Martin E. Schwab, Institute of Regenerative Medicine, University of Zurich and  
Dept. of Health Sciences and Technology, ETH Zurich

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Executive Summary – English	5
Executive Summary – Deutsch	7
Executive Summary – Français	9
<b>1. Background</b>	11
1.1 Opportunity for a bigger role of academia in translation	12
1.2 Call to action	13
<b>2. Academic translational medicine: definition</b>	14
<b>3. Identification of roadblocks in academic translational medicine</b>	15
<b>4. Academic culture for translation</b>	16
4.1 Translational medicine should be an asset rather than a risk	16
4.2 Importance of breakthrough science and the strengths of academia	17
4.3 Academia and industry are not speaking the same language	19
4.4 The challenge of measuring the efficiency of the translational process	20
<b>5. Academic support for translation</b>	22
5.1 Educate broadly and early	22
5.2 The importance of academic translational centers to support translational projects	22
5.3 Collaboration between researchers and technology transfer offices	27
5.4 Streamline the use of available funding	27
5.5 Infrastructure is not the primary gap	29
<b>6. Take home messages</b>	30
<b>7. Acknowledgements</b>	31
<b>8. Annex</b>	32
References	32
Box 1: Translational medicine	34
Box 2: Academic and post-academic support for translational projects	35
Box 3: Valley of Death	37
Fig. 1: Overview of the bench to bedside translational process	38
Fig. 2: The academia-industry continuum	38
Fig. 3: Perception of academic and industry partners by each other	39
Table 1: The main roadblocks to academic translational medicine	40
Table 2: Institutions supporting translational projects in the top five Swiss universities and ETHs (non-exhaustive).	41

4 Translating academic discover to patients' benefit: is academia ready to assume its key role?

## Executive Summary – English

### **Translating academic discovery to patients' benefit: is academia ready to assume its key role?**

It is long since acknowledged that academia does not translate research results into new medical therapies optimally, despite the huge resources invested in biomedical research. A vast majority of research results are never tested in humans, and very few academic life science discoveries are translated into a change in clinical practice, new medications, diagnostics, or devices. The difficulties of ensuring progression of basic scientific knowledge to patient benefit, and how to overcome the identified roadblocks are discussed in this paper.

We performed a literature search for the most common roadblocks faced by academic researchers and conducted interviews with translational project managers and representatives of institutions supporting academic translational medicine in Switzerland and abroad. The results served as a basis to highlight major roadblocks and lay the groundwork for recommendations on how academia could optimize its translational output. The report was reviewed and commented on by the Working Group for Academic Translational Medicine in Switzerland<sup>1</sup>, with representatives of the main academic translational initiatives.

Academia has a key role to play in translational medicine, but it is still insufficiently prepared to engage in a process that is arduous and risky, requires substantial funding, in-depth drug development knowledge, appropriate structures, and long development timelines. The two main areas in which we could see the most significant roadblocks in the translational process were academic culture and academic support.

To address the gap in academic culture, academia needs to:

- incentivize scientists to engage in translational medicine that is still perceived as a risk rather than an asset for an academic career;
- focus on breakthrough science and on the specific strengths of academia;
- speak the same language as industry and adopt industry standards, e.g. with regards to reproducibility and collection of data;
- develop new ways of measuring the efficiency of the translational process.

<sup>1</sup> The authors, in collaboration with: Leonardo Scapozza, Swiss Center for Therapeutics Discovery; Werner Enz, Basel Inkubator; Kostas Kaloulis, Catalyze4Life; Margrit Leuthold, ETH; Vincent Wagner, Accélérateur Translationalnel; Paolo Pagnetti, Lugano Medtech Center; Martin Kayser, Wyss Zurich; Uyen Huynh-Do, SITEM-INSEL.

To improve the academic support to translational projects, academia should:

- educate broadly and early on the translational process and challenges;
- develop academic centers with expertise in the translational process;
- optimize the collaboration between researchers and technology transfer offices;
- streamline the use of available funding and invest in essential infrastructure.

Our analysis of the current status of translational medicine in academia identifies important opportunities for improvement. This analysis is intended to be a basis for further discussions with the academic leadership and other stakeholders (e.g. politicians) to define and implement concrete measures on how to improve the situation in academia and draft a roadmap for more efficient and transparent collaboration between academia, public authorities, and industry.



## Executive Summary – Deutsch

### **Forschungsergebnisse umsetzen zum Wohl von Patienten: Nehmen die Universitäten ihre Schlüsselrolle genügend wahr?**

Schon länger besteht der Verdacht, dass Universitäten ihre Forschungsergebnisse in der Medizin oft noch besser in neue Therapien umsetzen könnten. Gleichzeitig werden aber bereits erhebliche Mittel in die biomedizinische Forschung investiert. Sehr viele Ansätze werden nie am Menschen getestet und nur relativ wenig neue Konzepte finden ihren Einzug in den klinischen Alltag, sei es als neues Medikament, diagnostisches Verfahren oder medizinisches Gerät. Dieser Bericht beleuchtet den komplexen und langwierigen Prozess der Umsetzung von Resultaten aus der Grundlagenforschung in die Anwendung für Patienten (auch Translation genannt) und diskutiert mögliche Lösungsansätze zur Überwindung der Hindernisse auf diesem Weg.

Wir haben dazu in einer Recherche zunächst die meist genannten Hindernisse dieser Umsetzung aus der Sicht der akademischen Forschung identifiziert. In Interviews haben dann anschliessend Projektleiter und Verantwortliche verschiedener nationaler und internationaler Forschungsinstitutionen diese Hindernisse bewertet und diskutiert. Die Interviews dienen als Basis für eine Beschreibung der grössten Hindernisse und für Empfehlungen, wie Universitäten die «Ausbeute» translationaler Forschung maximieren könnten. Der Bericht wurde evaluiert und angepasst von der Arbeitsgruppe für Translationale Medizinische Forschung<sup>2</sup> mit Vertretern der grössten Universitäten und Hochschulen in der Schweiz.

Die Universitäten haben eine Schlüsselrolle in der translationalen medizinischen Forschung. Sie sind aber oft nicht ausreichend gewappnet für einen solchen Prozess, welcher im Allgemeinen beschwerlich, riskant, langwierig und teuer ist, sowie spezielle Infrastrukturen und ausgewiesene Expertise in der Therapieentwicklung benötigt. Die Problematik betrifft zwei Hauptbereiche: einerseits die akademische Kultur und andererseits die Unterstützungsstrukturen an den Universitäten.

2 Die Autoren zusammen mit: Leonardo Scapozza, Swiss Center for Therapeutics Discovery; Werner Enz, Basel Inkubator; Kostas Kaloulis, Catalyze4Life; Margrit Leuthold, ETH; Vincent Wagner, Accélérateur Translationnel; Paolo Pagnetti, Lugano Medtech Center; Martin Kayser, Wyss Zurich; Uyen Huynh-Do, SITEM-INSEL.

Wir sehen folgende Verbesserungsmöglichkeiten im Bereich der Kultur an den Hochschulen:

- Es sollten mehr Anreize geschaffen werden, sich als Wissenschaftler in der translationalen Medizinforschung zu engagieren. Dies wird heute eher als Risiko denn als Chance für eine akademische Karriere angesehen;
- Konzentration auf hohe wissenschaftliche Qualität und die Stärken der akademischen Forschung;
- Der Sprache der Industrie mächtig sein und Industriestandards übernehmen, z. B. bei der Messung und Reproduzierbarkeit von Daten;
- Neue Methoden entwickeln zur Messung der Effektivität von translationalen Prozessen.

Zur besseren Unterstützung von translationalen Projekten an den Hochschulen sehen wir:

- Frühe und extensive Ausbildung in der translationalen Forschung mit ihren vielfältigen Herausforderungen;
- Entwicklung von universitären Zentren für translationale Forschung;
- Intensivere Zusammenarbeit zwischen Wissenschaftlern und Technologietransfer-Büros;
- Fokussierung der finanziellen Mittel und Investitionen in ausschliesslich essentielle Infrastrukturen.

Unsere Analyse der gegenwärtigen Situation zeigt Möglichkeiten auf, die translationale Forschung an den Hochschulen zu verbessern. Sie soll als Basis dienen für weitere Diskussionen mit den Leitungen der Hochschulen und anderen Interessenvertretern, z. B. Politikern, mit dem Ziel, die akademische Translation zu steigern und die Kollaboration zwischen den Hochschulen, den zuständigen Behörden und der Industrie effizienter zu gestalten.

## Executive Summary – Français

### Appliquer les résultats de la recherche académique pour le bien du patient: le monde universitaire est-il prêt à assumer son rôle décisif?

Il est reconnu depuis longtemps que le monde universitaire ne transforme pas de manière optimale les résultats de recherche en nouvelles thérapies, et ce malgré les énormes ressources investies dans la recherche biomédicale. Une vaste majorité des projets de recherche ne sont jamais testés chez l'homme et très peu de découvertes scientifiques en sciences de la vie aboutissent à un changement de la pratique clinique ou à la création de nouveaux médicaments, tests diagnostiques ou dispositifs médicaux. Les obstacles pour garantir que les connaissances scientifiques de base soient mises au bénéfice des patients ainsi que la manière de les surmonter sont abordés dans cet article.

Nous avons effectué une revue de la littérature pour identifier les obstacles les plus fréquemment rencontrés par les chercheurs et avons mené des entretiens avec des responsables de projets translationnels et des représentants d'institutions soutenant la médecine translationnelle académique en Suisse et à l'étranger qui ont noté chaque obstacle proposé en fonction de leur importance et expliqué leur score. Ces entretiens ont servi de base qualitative pour mettre en évidence les principales difficultés rencontrées et proposer des recommandations sur la manière dont les universités pourraient optimiser le transfert de leurs résultats de recherche. Le présent rapport a été examiné et commenté par le groupe de travail pour la médecine translationnelle académique en Suisse<sup>3</sup>, représentant les principales initiatives académiques pour soutenir la médecine translationnelle.

Le monde académique a un rôle clé à jouer dans la médecine translationnelle, mais il est encore insuffisamment préparé pour s'engager dans un processus ardu, long et risqué, nécessitant non seulement des connaissances spécifiques, mais aussi des structures appropriées et des financements substantiels. Nous constatons que la culture académique et le soutien apporté à la médecine translationnelle sont particulièrement inadaptés aux besoins actuels.

3 Les auteurs, en collaboration avec: Leonardo Scapozza, Swiss Center for Therapeutics Discovery; Werner Enz, Basel Inkubator; Kostas Kaloulis, Catalyze4Life; Margrit Leuthold, ETH; Vincent Wagner, Accélérateur Translationnel; Paolo Pagnetti, Lugano Medtech Center; Martin Kayser, Wyss Zurich; Uyen Huynh-Do, SITEM-INSEL.

Afin de faire évoluer la culture académique, le monde universitaire aurait besoin:

- d'inciter les scientifiques à s'engager dans la médecine translationnelle qui est encore perçue comme un risque plutôt qu'un atout pour une carrière universitaire;
- de s'appuyer sur la recherche de pointe et sur les forces spécifiques du milieu académique;
- de parler le même langage que l'industrie et adopter certaines de ses normes;
- d'utiliser de nouveaux moyens de mesurer l'efficacité du processus translationnel.

Afin d'améliorer le soutien académique aux projets translationnels, les universités devraient:

- former davantage de personnes, assez tôt dans le cursus universitaire, sur le processus translationnel et ses défis;
- créer des centres universitaires ayant une expertise en médecine translationnelle;
- optimiser la collaboration entre les chercheurs et les bureaux de transfert de technologie;
- rationaliser l'utilisation des fonds disponibles et investir uniquement dans les infrastructures essentielles.

Notre analyse de l'état actuel de la médecine translationnelle dans les universités identifie d'importantes opportunités d'amélioration. Cette analyse a pour but de servir de base à des discussions ultérieures avec les institutions académiques et autres parties prenantes (p.ex. les politiciens), afin de définir et mettre en œuvre des mesures concrètes pour améliorer le processus translationnel et rendre plus efficace et transparente la collaboration entre le monde académique, les pouvoirs publics et l'industrie.

## 1. Background

There is a general and longstanding consensus that academia does not translate research results optimally into innovative therapeutic approaches, despite the huge resources invested into biomedical research [1]. The difficulties of ensuring progression of basic scientific knowledge to patient benefit [from bench to bedside, Fig. 1] have long since been acknowledged [2]. Many so-called roadblocks have been identified as a cause for this poor translation [3–14], which will be further discussed in the present paper. Indeed, according to the U.S. National Institutes of Health, up to 90% of research projects fail before they are tested in humans [6], and less than 5% of all important life science discoveries made in academia are translated into a change in clinical practice, new medications, diagnostics, or devices [9].

However, there is no consensus on what should be considered an acceptable rate of translation, or even by which criteria successful translation should be measured. Available data show that only a minority of drugs on the market come from academia. Of the 252 new drugs approved by the U.S. Food and Drug Administration between 1998–2007, 61 (24%) originated in academia. Of these, 2/3 were further developed in a biotech company, and 1/3 in a pharmaceutical company [15]. While 13 new drugs came from Swiss pharmaceutical companies, none came from Swiss academia (some were partially attributed to Swiss universities) [15]. Similarly, in the European Union (EU), 17% of new active substances reaching the market between 2010 and 2012 were of academic or public body origin, or from a public-private partnership [16].

There is, however, a wealth of new technologies and products originating from academia. On average, there are around 260 patent filings (priority year, the date the first application is filed) per year in Swiss universities and ETH.<sup>4</sup> We estimate that 70% of projects coming from universities and 30% from polytechnic schools are in the field of life science.<sup>5</sup> Therefore, at the national level, at least 120 life science projects each year could potentially be further developed if they show promising preclinical potential. Of note, life science projects are responsible for over 90% of revenue for academia [17].

4 Estimation based on SwiTT reports 2013–2016 for the years 2012–2015.

5 Based on an analysis of 50 most recently published patents from five universities and two ETHs, up to 31 August 2017, on Espacenet.com. These estimations are consistent with numbers published by U.S. technology transfer offices, showing that 66% of start-ups and 65% of licenses coming from academia are in life sciences [17].

There is, therefore, a mismatch between what academia could develop, what it regularly promises, and what it actually delivers; academia frequently raises public attention and expectations in its mission to translate academic discoveries [18–20] and the high potential of its innovative projects. It is, therefore, high time that academia delivers on its promises.

## 1.1 Opportunity for a bigger role of academia in translation

Academia is currently poised to play a bigger role in the common effort to translate new discoveries. Indeed, pharmaceutical companies increasingly tend to focus their investments on the later stages of drug development (phase 2 and beyond), when substantial de-risking has occurred [6], and on key therapeutic areas [9], leaving a theoretical gap for the development of therapeutics originating in academia [Fig. 2].

This focus on later stages of drug development is due to the widely described increase in costs (trials, regulatory requirements, etc.), the decrease in profitability (end of blockbuster model, personalized medicine, patent cliff, earlier generics and competitor entry, etc.), and the need to focus on the value for shareholders (risk-aversion, focus on own therapeutic areas, mergers & acquisitions, etc.). Hence, there is a lower willingness to invest in early, high-risk phases of drug development, and a trend to leave to biotech and spin-off companies the role of de-risking the early stage projects [Fig. 2].

Some researchers may blame industry for this state of affairs, but there is a joint responsibility here: although academia and industry have different objectives, they should share the same vision, which is to bring new therapies and drugs to patients in need. With this objective in mind, coordination between these two players is essential. It is important to note that the pharmaceutical industry (and to a lesser extent small specialized companies) are the only players that further develop drugs, manufacture them and make them available for patients. It is, therefore, understandable that industry tends to shy away from investing in early-stage research in favor of developing compounds with established indications of viability, such as proof-of-concept [14]. Additionally, it seems obvious that the pharmaceutical industry cannot support all academic projects that might have some potential (often based on the subjective opinions of the researchers themselves); industry has to focus on projects that already show some evidence of potential, and on projects that are within their areas of interest and competence.

There is evidence that the pharmaceutical industry and academia are increasingly collaborating. Pharma has been initiating partnerships, both launching «science hubs» with academia (such as Pfizer's Centers for Therapeutic Innovation or GSK's Tres Cantos Open Lab Foundation), or supporting innovative projects in academia (such as GSK at Harvard, or AstraZeneca at Columbia) [21]. Academia has been establishing academic drug discovery centers (ADDC) and academic translational centers (ATC) (such as SPARK at Stanford, QB3 at University of California, or Brigham's Translational Accelerator). These initiatives could serve as paradigms. In Switzerland, despite some delay compared with the United States, several similar initiatives are being created (translational centers, incubators, grants, associations, etc.) with the goal of improving translational medicine, as discussed below.

## 1.2 Call to action

We believe that academia has a key role to play in optimizing translation of its discoveries, but that it is insufficiently prepared to engage in a process that is extremely arduous and risky, requires substantial funding, in-depth drug development knowledge, appropriate structures, and long development timelines. Academia also has the responsibility to streamline and coordinate these efforts, in particular because resources are limited and because most funding comes from public sources.

Based on the authors' previous experience in academic translational research and in industry, on international experience, on literature, and on interviews with stakeholders, we deliver a critical situation analysis of translational activities in academia, and we outline some possible solutions for improving the current situation. This analysis is intended to be a basis for further discussions with academic leadership structures and other stakeholders (e.g. politicians) to define and implement concrete measures on how to improve translation in academia and draft a roadmap for more efficient and transparent collaboration between academia, public authorities, and industry.

## 2. Academic translational medicine: definition

Translational medicine is often referred to as the transition from «bench to bedside», taking basic research concepts, methods and results to the clinical level, with the goal of proving the efficacy of a new treatment [Fig. 1]. In reality, translation in medicine covers a much broader spectrum, and also includes transitions from «bedside to practice», linking clinical research with clinical care (best practices) [13], from «practice to population health» [22], and from «population to global health» [23,24]. At each level, the information collected in turn feeds basic research to further improve the current standard of care [Box 1]. This means that the best possible therapy is of no use if it is not implemented as standard of care, and that efforts following proof of treatment efficiency should be sustained or even increased to improve its implementation within society [25].

This article focuses on the first phase of translation (from bench to bedside), which in part takes place in academia. This «academic translation» represents the phase during which projects, coming from basic research, with a potential to target an unmet medical need, are further developed within academia to confirm their potential and raise interest for further development, often by the private sector. Academic translational medicine can include, but is not limited to, patenting, production of pre-clinical data to support translational potential, disease model validation, human cell- or tissue-derived models, bioinformatics, translational pharmacokinetics and pharmacodynamics (PK/PD) [26], animal toxicology studies, manufacturing of small batches, early development planning (e.g. pre-clinical, clinical, manufacturing, regulatory and business plans), industry relations, preparation for incorporation (e.g. into a spin-off company), and even first-in-human clinical studies.



### 3. Identification of roadblocks in academic translational medicine

To identify the critical steps in academic translational medicine, we analyzed which are the most common roadblocks that academic researchers face. We first listed the most frequent roadblocks cited in the literature [3–14] and conducted interviews, in which participants had to rate each roadblock according to their perceived importance (from 0 to 10) and explain the rationale for their score. Interviewees could also add roadblocks that were not mentioned. Averages were calculated and presented in order of the most frequently identified roadblocks.

We interviewed people who managed translational projects (n=10) and representatives of institutions that support academic translational medicine in Switzerland and abroad (n=10). The report was then reviewed and commented on by the Working Group for Academic Translational Medicine in Switzerland. The method does not claim to be a strict statistical analysis; the interviews served as a qualitative basis to identify major roadblocks and to discuss and propose possibilities for improving academic translational medicine.

The identified roadblocks to academic translational medicine and their average ranking are presented in Table 1. There was a general agreement by responders that the list was complete, and no other major roadblocks were identified. Only slight differences (>2 points; <3 points) were seen between interviewee groups (bioentrepreneurs versus institution representatives): while entrepreneurs were more concerned with academic and regulatory procedures, and non-reproducibility of data, institution representatives were more concerned with the lack of academic culture and motivation.

We identified two main areas in which the roadblocks ranked high, namely *academic culture* and *academic support*. Academic culture includes, among others, the gap with industry expectations (ranked 1), the lack of industry network (ranked 4), and the lack of incentive (ranked 7). Academic support includes the lack of funding (ranked 2), the lack of academic resources (ranked 3), the lack of education (ranked 5), and the lack of expertise (ranked 6). The discussion below presents the authors' analysis of the current situation, based on the roadblocks identified in the literature and discussed in the interviews, as well as the authors' experience in translational medicine and industry.

## 4. Academic culture for translation

### 4.1 Translational medicine should be an asset rather than a risk

One of the limitations to fully engage in translational medicine often mentioned by researchers is the conflict with their ongoing career («risk of career damage» [1]), in particular the drawbacks associated with the lack of publications, the lack of «prestige», and a promotion system that does not reward translation.

Indeed, some senior researchers involved in translational research deplore that it is still sometimes seen as poor science, and that translational medicine is not considered strongly basic science driven. They, therefore, acknowledge that it would be very difficult to only focus on translational research, as they need to be significantly involved in basic science to uphold their reputation. Unless they have huge resources and undisputed credit within their institution, translational research then becomes a part-time hobby when their basic research delivers adequately and their career is assured. This implies a huge lack of time and resources for translational science, which might in turn contribute to the feared lack of quality.

A similar situation can be seen with clinicians, who are often requested to demonstrate that they perform in their clinical activities before being able to invest time and energy in translational research. Like fundamental researchers, they have to keep up with an increasingly complex and large body of literature, while their translational efforts are not rewarded as highly as the more classical measures, such as number of publications, journal impact factor, or grants awarded [6]. Another challenge regarding scientific credibility is the feeling of mistrust that can be conveyed to the scientific community if a group regularly publishes overly positive data on a drug, marker, or diagnostic when they are themselves the inventors of the patent or the founders of a company using the technology.

Some researchers argue that translational science cannot be well published, but this position is debatable. It very much depends on the subject and on the phase of translation: a convincing well-conducted animal proof-of-concept study can reach high-ranked journals. On the other hand, manufacturing process development, formulation and PK studies, and standard good laboratory practice (GLP) toxicology are indeed more difficult to publish in peer-reviewed journals. Moreover, as for basic science, failures are rarely published. Reporting failures is, however, an efficient mode of drug and target selection, improves translation, and provides teaching examples for young researchers [6].

Many academic researchers are also concerned with the delay in publication that patent filing can induce, with the fear that other groups will publish first. Moreover, they could have a «gap» in their publication record if the delay is too long. The publication issue is particularly critical for young researchers. The very long timeline to show impact, the difficulty in publishing data in high impact journals, and the potential delay in publication are incompatible with the careers of young researchers, who only have a few years to establish their credentials as creative scientists worthy of tenure [6], according to strictly pre-defined academic publication criteria. Delaying publication can also be a major problem for master and PhD students, who need these publications to obtain their degree and move forward with their career. Collaboration with industry can induce additional delay in publishing, or even censor publication of some results.

Younger academics are often pushed to choose between engaging in translation (with difficult return to basic science in case of failure) and pursuing an academic career. Promising researchers might therefore shy away from translational medicine.

Academia should incentivize scientists to move outside their comfort zone, which implies exposing them to a lot of unknowns, such as a complex regulatory environment, patent regulations, manufacturing procedures, or business constraints. It could promote the engagement in translational projects by rewarding patenting, licensing or publication in translational journals (beyond impact factor), creating career tracks in translational medicine or facilitating the management of a «double» career (translational research together with basic research or clinical activities).

## 4.2 Importance of breakthrough science and the strengths of academia

As for any type of translation, be it a text or science, the quality of the original has to be good. Therefore, investment in basic science is essential, and a prerequisite for translation to occur. Academia must find an equilibrium between time devoted to translational research and time devoted to basic research [5, 27, 28].

While it is important that researchers acquire commercial skills and mindset, these assets should not overshadow the fact that the science has to be truly innovative and compelling: business expertise can easily be brought to a scientific project (by training researchers or in-sourcing expertise), but the contrary is almost impossible (i.e. science cannot be «invented» by a very entrepreneur-

ial team). Lack of good quality science will eventually become evident when a pharma company or venture capital firm performs in-depth due diligence, causing considerable loss of time and credibility. Additionally, neglected scientific fundamentals (poor understanding of target disease biology, misleading animal models for human efficacy, etc.) will significantly contribute to the risk of failure in late clinical stages of development.

Industry has incomparable strengths in clinical development, manufacturing, and marketing, against which universities should not try to compete [5]. The strengths of academia lie in areas in which industry R&D might not necessarily focus:

- **High-innovation projects:** many innovations might simply not be in industry's pipeline because of the breadth of academic cutting-edge research. High throughput screening techniques and all the «omics» are generating such a large volume of data and potential drug targets that they cannot all be processed by the pharmaceutical industry [1].
- **High-risk projects:** industry might not develop such projects from scratch, which are often the result of passionate, pioneering, and rightly stubborn basic or clinical scientists (e.g. CAR-T cell therapy originated in academia [29]). Academia also does not have to target highly profitable projects and faces no pressure for short-term profits.
- **Serendipity:** researchers can allow themselves to «follow the science»; if it leads them elsewhere, they might as well develop the candidate for another indication or application, or continue working on the project for the sake of science. Contrary to industry, academia has no particular obligation to develop innovation in pre-defined therapeutic areas.
- **Rare and neglected diseases:** while some have been targeted by industry, often as a proof-of-concept for a follow-on indication with a larger market, treatments for many rare and neglected diseases are yet to be explored.
- **Not-for-profit projects:** these might not have a direct commercial impact, but can provide benefit to society overall (e.g. an alternative treatment with lower costs).

- **Repurposing of known drugs:** this is often not interesting for the pharmaceutical industry, as it might potentially have an impact on the price or safety profile of already marketed products.
- **Use of clinical databases (biobanks, registries, etc.):** these are concentrated in academia. Databases attract a lot of attention from the pharmaceutical industry, and academia has a unique opportunity to develop and access them.

Academia should, therefore, focus on its strengths. Importantly, however, even if academia has no comparable pressure on return on investment, and can support high-risk or not-for-profit projects, it cannot and should not invest the limited available funding for translational research in projects that lack rationale or potential. Stringent and professional selection should be in place, and projects that do not qualify for translation should be redirected to basic research, where they also have a chance of successful development [5].

### 4.3 Academia and industry are not speaking the same language

There is too often a mismatch between what academia and industry think of each other [Fig. 3], with many preconceived ideas and a lack of common language and understanding. While they have different incentives and constraints, their goal should be the same, which is to bring new therapies to patients. Therefore, both should focus on how best to interact with the other partner and find a common ground, complementarity, and at best, synergy.

One of the main difficulties mentioned by academic researchers is how to make their research attractive for industry [Table 1]. In initial discussions, the pharmaceutical industry usually finds projects interesting but incomplete, and will ask for more data, in particular proof-of-concept data and human data. In addition, industry might also find the drug candidate less attractive, because it is still a poorly characterized new chemical entity, because industry has little or no experience with this kind of compound, or because it addresses a clinical indication that is known to be difficult (e.g. Alzheimer) [27]. The pharmaceutical industry also expects to see a very clear and streamlined strategy on how the group plans to go forward to reach a clinical proof-of-concept and ultimately a market. The plans should include clinical, regulatory, reimbursement, manufacturing, and intellectual property strategies.

It is often mentioned that a majority of the results from academic laboratories cannot be reproduced when repeated in industry laboratories [4, 7]. Academia blames industry for not following their protocols, not understanding them, or simply being incompetent. The industry might believe that researchers, under the «publish or perish» pressure over-interpret (in terms of scientific significance or clinical relevance) or, worse, embellish their results [3]. There may be an element of truth in both cases; industry might not have the same level of expertise as academic laboratories, and might even outsource confirmatory studies to contactors that may not have the capacity to reproduce a specific model that took years to establish in academia. On the other hand, results could be judged as extremely positive and relevant in academia, while the industry would have higher expectations to take the financial risk to further develop a product [3].

To communicate with industry, researchers from academia need to speak the same language as industry and to adopt industry standards, addressing both market opportunity and risk mitigation, in order to appear more attractive to risk averse potential acquirers and regulatory bodies [13]. To facilitate transfer to industry, the mindset in academia should be that the further a project progresses, the more industry-compatible experiments should be (e.g. GLP or good manufacturing practice (GMP) standards), and the more professional the project management should be. Even in early stages, the introduction of a good quality management system will be beneficial.

#### **4.4 The challenge of measuring the efficiency of the translational process**

According to the European Federation of Pharmaceutical Industries and Associations (EFPIA), the average time for a drug to reach the market (from patent application to market) is around 12–13 years [30], and is probably much longer for academia. It is, therefore, very difficult to measure the final output of translation, since it does not boil down to a simplistic publication count [1], nor can it be defined in terms of drugs produced or first-in-human trials, because of the long timelines associated with getting a drug to the market [5]. Moreover, translation is a combined effort (academia, spin-off, industry, etc.), and it is difficult to identify the single contributions in the shared collaborative process [31]. The lack of valid performance indicators also precludes comparisons between academic institutions or between countries.

While it is extremely difficult to measure performance of translational medicine, many centers use some indicators. For technology transfer offices (TTOs), the major metrics are the number of patents filed, the gross licensing revenue (though that can be overshadowed by a revenue from a blockbuster product developed many years ago), the number of licenses, and the number of startups [17]. Some have suggested to measure output of academic translational centers by counting patents, clinical trials, and collaborations with industry [1]. Life sciences research institutes, such as the VIB center in Flanders, Belgium, track the number of publications, patents, income from industrial collaboration, creation of startups, authoring of PhD theses, and capacity to attract industrial and international funding [32]. Stanford University's School of Medicine SPARK Translational Research program measures its performance with the number of projects entering clinical phase and/or being out-licensed [33].

People working in translation should not be evaluated according to standard academic indicators; business-related performance indicators could be used, such as milestones definition and achievement, and the ability to work in multi-disciplinary groups [1]. Deliverables that bring strong support to the team and help them focus, such as the articulation of a target product profile [5], a meaningful Gantt chart (a visual view of tasks scheduled over time), or an in-depth population-to-sale analysis, could also be ways of measuring short-term output.

## 5. Academic support for translation

### 5.1 Educate broadly and early

There is much room for improvement in collaborations between stakeholders (researchers, clinicians, industry, authorities, etc.), because of a lack of education on the processes and challenges of translational medicine. The education offered today to students in life science is scarce, not coordinated, and often focuses on general entrepreneurship concepts.

If some take the view that it is not the role of academia to train students to translate their work, they should remember that, eventually, only a small minority of students will have an academic career, and that it is the academic mission to prepare them for an alternative career (e.g. in industry); education therefore teaches students and researchers about the drug development process and also indirectly educates industry on the nature of academia's contribution to the process [27].

Academia should at least teach an overview of the translational process (including its challenges and pitfalls) to all students in life sciences, while a more advanced curriculum in translational science should be available for more advanced students, in particular those engaging in translation. Early sensitization to the translational process and to the need to work in multidisciplinary teams should influence the culture and the mindset of young researchers: they might in future more easily realize the potential of a bench discovery that would have otherwise stayed on the bench, be aware of what it takes to engage in a translational project, collaborate more efficiently with other researchers involved in translation, or avoid unintentionally disclosing innovations.

### 5.2 The importance of academic translational centers to support translational projects

The importance of forming multidisciplinary teams cannot be understated. Long gone is the nostalgic time when scientific innovation was single-handedly powered by a physician-scientist working alone [1]. Groups should be aware that they will need to form interdisciplinary teams with experts working outside their own areas of expertise, with other professional competencies, such as patent and corporate law, reimbursement, pricing or regulatory matters [13].



It is important to constitute early an interdisciplinary team, at least a «virtual» one, or join a central platform with experts in translation. Not only will it enable the researcher to make early adequate choices and avoid to repeat «classical» mistakes, it will also be key to convincing funding bodies and investors. In our opinion, three critical hands-on types of expertise have to be available within a successful medicine research team:

- **A project manager.** Efficient project management as part of the multidisciplinary team helps drive rapid project progress [13]. Project management skills represent one of the biggest gaps of researcher expertise [Table 1]; they will realize that the level of project management/planning requested by industry or venture capitalists is much higher than what is needed for a grant proposal. A multidisciplinary translational team needs someone who can coordinate all the experts, while keeping the end goal in mind. Experts (legal, regulatory, etc.) can easily be found, but they have to be coordinated. Ideally, the project manager should have previous experience in the process.
- **A mentor.** Ideally, the new bioentrepreneur can be mentored early by a professor with hands-on experience in drug development. The mentor will be able to give relevant advice and close coaching, be more likely to have a useful network that will further advise on development and facilitate fundraising, invest more group time and money in the project, and support a longer collaboration (e.g. via Innosuisse grants in partnership with the newly created spin-off). Their track record in developing successful translational projects will also be very important for both early and late funding. If the researcher is in a group with limited expertise, they might benefit from the large network of «start-up» coaches (e.g. Innosuisse). However, these coaches have no personal stake or investment in the process, and the researcher might want to establish a closer partnership with an experienced entrepreneur, for example as a co-founder.
- **A clinician.** As part of a basic research team, a clinician can help consider translational opportunities, and understand a genuine clinical need that may not necessarily be intuitive for a basic scientist [27]. Here lies an important advantage of academia over industry, where interaction with clinicians is easy and frequent; it should be exploited to understand early how the product can best be tested and implemented in a clinical setting. Clinicians can also facilitate the incorporation of the patient perspective (research questions, study design, patient recruitment, etc.) into the product development.

Because it is often difficult for the young bioentrepreneur to find experienced project managers, clinicians, and former entrepreneurs who are willing to join the project, academic centers have a key role to play in supporting the bioentrepreneur in these first steps of development. Furthermore, besides these three critical hands-on types of expertise, the project may need other competences at an early stage, such as pharmacokinetics, medicinal chemistry, and regulatory affairs that have been developed in industry but neglected in academia. Academic centers have a key role to play in supporting the bioentrepreneur in these first steps of development, in the form of a centralized platform.

The appearance of academic structures that specifically support translational projects is a rather recent phenomenon [Box 2]. One of the first such centers worldwide is the Institute for Translational Medicine and Therapeutics (ITMAT) at the University of Pennsylvania, which was founded in 2004 [31]. While some main academic translational centers appeared in the United States between 2005 and 2010 (e.g. SPARK at Stanford was created in 2006, and Harvard Catalyst, the Harvard Clinical and Translational Science Center was established in 2008), Swiss academic translational centers only appeared in the last few years (almost two decades after the creation of the first TTOs) and are still in a process of development. These centers are very diverse in their setup, stakeholder group, goals, and resources. While some are purely academic (e.g. Therapy Development Accelerator), most result from a partnership between academic, public (cantons, City, State) and private (foundation, industry) institutions (e.g. Base-Launch; SITEM) [Table 2, Box 2]. Some have the primary mission to support local institutional academic translational medicine projects, while others also aim to attract projects from around the world, thus participating in the economic promotion of their region.

In terms of the role academic structures should fulfill, we think that academia should build dynamic platforms that coordinate private, public and academic initiatives and institutions, both at the national and international levels, to sketch out the most efficient way to develop a particular drug. For projects at a very early stage, academia should provide expertise and consultants to address needs in a tailored manner. Whether they are called academic drug discovery centers (ADDC) or academic translational centers (ATC), an academic structure supporting translation should provide at least the following support [Box 2, Table 2]:

- **Sanity check.** An academic center should be able to manage expectations and to provide an unbiased evaluation of the project's potential (in terms of science and marketability) and help researchers focus on the most promising translational steps.
- **Project management and strategic planning.** The center should help the researcher acquire a sound overview of the process, identify early the potential pitfalls they will encounter, and help draft a preliminary financial, business, regulatory, manufacturing, and/or clinical plan. Academic structures supporting translation should help researchers to adopt professional processes and standards in project management, such as the precise definition of the target product profile (TPP) and the meaningful use of Gantt charts to guide development. Centers should also advise bioentrepreneurs on how to find the key team members needed for project development and completion (project manager, seasoned entrepreneurs, and clinicians, as discussed above).
- **Mapping of the ecosystem.** By constant interaction with all stakeholders and researchers, the centers will acquire a deep, constantly evolving, and unique knowledge on the ecosystem that will steadily be updated by experience and that will stay within academia. Centers should map available academic resources (medicinal chemists, safety experts, high-throughput facilities, etc.) and identify the best third parties for outsourcing, pre-negotiate conditions (e.g. timelines and pricing), and monitor their performance.
- **Industry relations.** The academic center will be in contact or initiate contact with the most adequate industry partners to initiate discussions on the project, raising interest and validating the development plan early. Contacts between academia and industry are usually not structured, and depend heavily on personal connections. In Switzerland, researchers often have connections with local Swiss companies such as Roche or Novartis, due to their proximity and to the fact that many people transition from one company to another and from academia to industry. However, researchers tend to have relatively poor connections with international partners (e.g. US-based pharmaceutical companies). Therefore, academic structures supporting translation need to expand the network of industry relations and to provide a structure that nurtures these relations.

- **Investor relations.** Academic structures supporting translation will direct the researcher to the right investors at the right stage of the project. Due to lack of experience, bioentrepreneurs often apply for funding in the absence of a well thought-out strategy, without taking into account the stage or therapeutic area that could be of interest for the funding body. It is, therefore, relatively common for researchers heading projects with almost no pre-clinical data to contact venture capitalists or pharmaceutical companies who will have to send them back to the bench. This process is unnecessarily time-consuming for both parties, reflects poorly on academia (lack of professionalism, reliability, and credibility), could compromise partnerships with potential investors and partners, and discourages bioentrepreneurs.
- **Project mining.** Finally, academic centers could also help to «mine» academic institutions for projects. Indeed, not all basic researchers recognize their ideas and data as being amenable to translation and may never pursue their projects along these lines [5]. This «active mining» could be done by experts from translational centers, for instance by attending and sponsoring departmental seminars and scientific meetings, and meeting informally with researchers at regular intervals.

It is important to note that one should not confuse this tailored extensive support with «baby-sitting»: bioentrepreneur expertise should also be acquired the «hard way», through experience and deepening knowledge (reading, conferences, discussions), without expecting all solutions to be resolved by external support.

Efforts by institutions should be coordinated to avoid cannibalism of resources. Coordination between translational centers is also required to promote synergies (competences and equipment do not need to be in all centers, in particular for Switzerland, a country of 8M inhabitants). The very decentralized model in Switzerland, as seen by the prominent role of cantons, both in education and economic promotion, might favor a coordinated matrix-based translational center system. In the short term, we suggest close collaboration, communication, best-practice sharing, and alignment between centers, with the possibility to collaborate or even transfer projects when a given expertise is greater in another center.

### 5.3 Collaboration between researchers and technology transfer offices

Close collaboration of academic centers with TTOs is essential. Academic centers should be able to perform an early review of invention disclosures with the TTOs, while orientating the group to the TTO for any matter regarding intellectual property.

On the researcher's side, it is interesting to note that the perception of TTO varies a lot, and depends on the researcher's experience. In general, researchers are satisfied with the work done around the patent. This level of satisfaction has a lot to do with expectations: those who expect filing and management of the patent are usually very satisfied, whereas those expecting overall «technology transfer» too literally in the form of extensive project support are disappointed. Another point of friction can be license negotiation a few years later, when a spin-off company is created; the researchers switch roles (from academics to entrepreneurs) and have to negotiate with the TTO. While some researchers complain about the unfavorable conditions offered by academia or the lack of expertise in negotiation and industry know-how, TTOs point out unrealistic expectations by researchers with no experience in out-licensing. This can lead to major delays and be a roadblock for the spin-off, which cannot start funding negotiation without a license from academia.

In order to optimize collaboration between newly created spin-off companies and TTOs, on the one hand, TTOs could be more flexible on negotiation, more transparent (e.g. publish benchmark) and communicative, by explaining the rules and limits of negotiation. On the other hand, to facilitate negotiation, the newly created spin-off could rely on an independent expert to negotiate on their behalf, such as an intellectual property lawyer.

### 5.4 Streamline the use of available funding

Investigators are prompt to point to funding as being the «elephant in the translational research room» [6]. There is a point during translational development, termed the «Valley of Death», when funding switches from an academic source to funding by industry and investors [Box 3]. A challenge is that many translational activities, often linked to regulatory requirements, are not perceived as highly scientific (e.g. establishing a GMP manufacturing process or performing GLP toxicology). These have a low potential for publication and do not attract funding from public sources. They are, however, indispensable for bringing any

discovery to the market, whether the drug originates from academia or industry. It can be argued that these activities should be funded by industry. However, industry neither has the obligation nor the strategic interest to fund every academic project. As pointed out by Yu, we sometimes reach a «chicken and egg» scenario, in which investors need proof-of-concept data to invest in the further development of basic research, and researchers conversely need funding for their discoveries to achieve proof-of-concept [14]. To enhance progress in medicine, it is up to academia to de-risk its own projects by advancing them to disease-relevant proof-of-concept, with pharmacokinetic and toxicology studies. This will not only make their projects more appealing to the biomedical and pharmaceutical industry and investors, but will also increase chances of reaching the market and getting a product to the patient.

At the very early stage of academic translation, smaller scale funding is described as relatively easy to obtain in Switzerland: there are indeed a lot of start-up competitions (e.g. Mass Challenge), grants (e.g. foundations, Innosuisse), local academic support (e.g. grants to young researchers, grants for translational projects), and other philanthropic initiatives (e.g. Wyss Zurich, Wyss Center Geneva).

When higher amounts of funding are needed to initiate translation within academia, most researchers wish for higher governmental support. The Swiss National Science Foundation (SNSF) and Innosuisse initiated the BRIDGE program to fill the gap they identified between SNSF (basic research) and Innosuisse (applied research) funding schemes. However, the number of funded projects is limited, and often considered by researchers as insufficient compared with other countries (e.g. Germany, United States, Israel), although objective comparison is complicated by lack of data and the diversity of funding mechanisms. In 2017, BRIDGE distributed CHF 2.5M for life science projects. In comparison, the SNSF distributed CHF 407M for basic research in biology and medicine, and CTI/Innosuisse attributed CHF 36M for life science projects (source: BRIDGE, SNSF and Innosuisse reports).

Groups will face most issues when trying to complete their first significant round of venture capital financing (Series A funding), when higher amounts are discussed, international competition starts, and new stakeholders are involved. Further rounds are even more difficult to navigate, in particular in Switzerland [see Valley of Death, Box 3], but are beyond the scope of this article, because most projects are incorporated into a spin-off at the time of the first round of financing.

Academia should support all activities associated with research translation, both the science (e.g. the first pre-clinical experiments that can still be well published), but also the necessary processes (reproduction of data, GMP manufacturing, GLP toxicology, etc.) that cannot be published, which are difficult to fund but are essential for successful translation [34].

## 5.5 Infrastructure is not the primary gap

Standard infrastructures such as GLP- and GMP-facilities are often considered unnecessary, because the corresponding work can easily be outsourced, particularly in Switzerland where the offer is large (hospitals, translational centers, contract research organizations (CROs)). However, CROs may not welcome very small projects (e.g. a single batch of a new experimental drug), unless there is a clear plan for future collaboration, and/or may charge excessive amounts. Therefore, infrastructure can be outsourced, but at high cost. Additionally, the academic project might not rank high on the priority list of major CROs, thus generating delays. This becomes very relevant when the manufacturing steps are not well defined, and a lot of concerted discussions are needed, as is the case for new technologies in an early stage of development. In such cases, academic facilities with unique expertise such as Wyss Zurich, specialized in innovative tissue or cell therapies, or UCLA's Human Gene and Cell Therapy Facility, offer a welcome service and retain all the process knowledge within academia.

Offering facilities to selected projects can be a way of accelerating translation, but this requires extremely well organized infrastructure and highly qualified staff (note that industry salaries and opportunities make it difficult for academia to recruit). It is rather unlikely that an academic facility can be as cost-effective as a CRO, with high expertise, economy of scale, and numerous customers. If the setting is not optimal, it would therefore be a costly way of financing projects.

## 6. Take home messages

Our search for the most common roadblocks to academic translational medicine identified two main areas in which the roadblocks ranked high, namely *academic culture* and *academic support*. Academic culture includes the gap with industry expectations, the lack of incentive, a misalignment between translational objectives and the academic reward system, and the lack of industry network. Our academic mindset towards translational medicine urgently needs updating: translational research should be considered an asset for an academic career, rather than a risk. Academia can exploit areas in which industry R&D does not focus, such as high-innovation projects, high-risk projects, rare and neglected diseases, not-for-profit projects, repurposing of known drugs, and use of clinical databases. Moreover, academia must learn to speak the same language as industry and adopt industry standards, thereby making research attractive for industry and providing proof-of-concept data, human data, and/or clinical evidence. Academic researchers should keep the end in mind, rather than the measure of the translational process, or else innovative or high-risk projects may be biased against; there should be no focus on financial gain.

Identified roadblocks to translation that fall into the academic support category include lack of funding, lack of academic resources, lack of expertise, and lack of education. Better collaboration between stakeholders can be achieved by improving the quality of education on the processes and challenges of translational medicine. Academia should establish translational hubs to broaden networks and form multidisciplinary teams, and build dynamic platforms that coordinate private, public, and academic initiatives and institutions, both at the national and international levels. For early stage projects, academia should provide a facility to manage expectations, assist with project management and strategic planning, map available academic resources, help to identify the best third parties for outsourcing, and initiate/expand industry relations. Academic structures could also provide support with investor relations and encourage a culture of collaboration between academic centers, researchers, and TTOs. Finally, available funding must be streamlined for academia to de-risk its projects.

Our analysis of the current status of translational medicine in academia identifies important opportunities for improvement to ensure better translational rates, and provides the groundwork for discussion and creation of measures that will help to translate basic scientific knowledge to patient benefit.



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## 8. Annex

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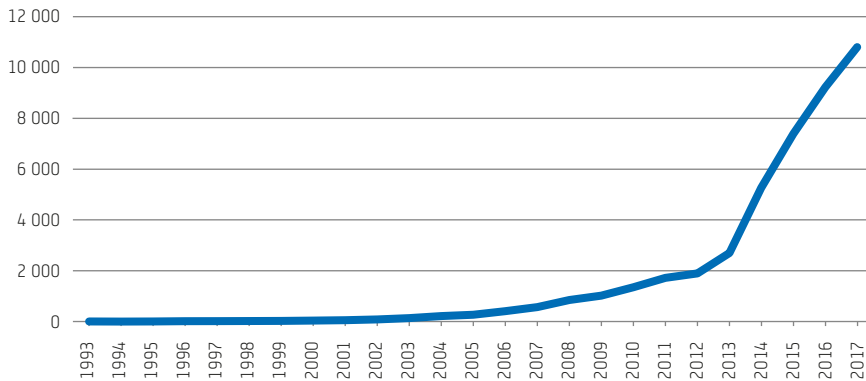
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## Box 1: Translational medicine<sup>1</sup>

The term «translational» first appeared in PubMed in 1993, and its use remained low for about ten years, after which it has been used in an exponentially increasing number of publications [1].

**Number of PubMed results by year for the terms translational medicine/science/research**



There are many definitions of translational medicine [1, 31]. The concept is, however, always similar, and involves bringing new inventions generated in the laboratory to the patient and to society, with the objective of improving human health. Translational medicine is described as an interdisciplinary branch of the biomedical field supported by three main pillars: benchside, bedside and community. At each level, the information collected will in turn feed basic research to further improve the current standard of care. Its goal is to combine disciplines, resources, expertise, and techniques within these pillars to promote disease prevention, to enhance diagnosis and therapy [35]. Translational medicine includes the multidisciplinary process from basic science through to manufacturing, regulatory, clinical testing all the way to market. It encompasses aspects of basic science and clinical research, requiring collaborative skills and resources that bridge basic laboratory and clinical settings [13]. Translation has been equated to innovation, or «value-creating novelty», with a specific end goal of clinical utility [6]. Similarly, translational medicine has been described as the application of scientific method to address and improve a health need, e.g. by reducing disease incidence, morbidity, and mortality [36].

<sup>1</sup> For the purposes of this article, the terms translational medicine, translational research, and translational science are interchangeable.

## **Box 2:** Academic and post-academic support for translational projects

### **Academic Drug Discovery Centers**

- Academic Drug Discovery Centers (ADDC) couple the curiosity-driven research culture in academia with rigorous preclinical drug discovery practices used in industry [5]. They provide the scientific expertise required in domains such as assay development and compound discovery and optimization, which most biologically-oriented principal investigators do not have [5].
- There is no formal ADDC in Switzerland to our knowledge, but informal academic networks such as the University of Zurich Drug Discovery Network (UZH DDNZ) are available.
- International examples of ADDC include the University of Minnesota's Institute for Therapeutics Discovery & Development (ITDD) or the Tri-Institutional Therapeutics Discovery Institute (Tri-TDI) in New York, and the Academic Drug Discovery Consortium provides an interesting interactive web-based platform to build collaborative networks among university-led drug discovery centers and programs.

### **Academic Translational Centers (ATC)**

- Academic Translational Centers (ATCs) support bioentrepreneurs with guidance and training on development and commercialization of inventions [7]. The main goal of these structures is to support and develop the projects from the institution itself.
- In Switzerland, there are only a few academic translational centers specifically supporting the development of translational projects (Table 2); in Zurich, ETH offers the ielab for around ten young researchers per year selected to receive a Pioneer grant to develop their project (about 1/3 in life sciences), while the Therapy Development Accelerator (TDA) of the University of Zurich offers professional services to all students, staff, and faculty, providing analysis and management of translational projects. Also in Zurich, Wyss Zurich supports projects from UZH and ETHZ in the field of regenerative medicine and robotics, thanks to a generous donation from entrepreneur Hansjörg Wyss. At EPFL, Catalyze4Life supports the projects with both funding and advice. In Geneva, the newly established Accélérateur Translationnel pursues the same objectives.
- International examples of ATC include SPARK at Stanford, and the Brigham Translational Accelerator institute.

### **Technology Transfer Offices (TTOs)**

- There are technology transfer offices (TTOs) in all universities (Unitetra for Zurich, Basel and Bern, Unitec in Geneva, PACCT in Lausanne, see Table 2) and ETHs. The TTOs mainly assist researchers with the protection of their idea, most often by filing a patent. They are also in charge of reviewing contracts between industry and academia. Moreover, they negotiate licensing rights with companies (newly created spin-off or existing company) that want to use the intellectual property developed at the academic institution.
- Of note, most TTOs do not have the goal of developing specific projects until they mature to spin-offs, nor do they support spin-offs in their early development. This role is usually given to ATCs (see above).

### **Clinical Trial Centers (CTC)**

- Most academic centers have Clinical Trial Centers (CTC), which are coordinated by the Swiss Clinical Trial Organisation (SCTO). A clinical trial center supports the research teams in the planning and execution of clinical trials in compliance with local regulations and international standards (Good Clinical Practice standards, GCP), for example providing facilities such as an equipped clinical research ward for trial patients, and support in data management, monitoring, or GCP training.
- CTC services are primarily offered to support academic and investigator-initiated clinical research, but are also open to industry-sponsored projects. While they come into play late in the translational process, when groups are ready to proceed into trials in humans, they also should be involved early (e.g. to provide support for the clinical plan).

### **Incubators**

- Incubators are organizations nurturing new ventures in their early development, through targeted resources and services that can include low-cost or free office and laboratory space, coaching, common services, and networking connections. Incubators can support ventures before (early incubators), during, or after their incorporation. They take little or no equity, as they are usually funded by the government or other institutions. Incubators might be linked to funding bodies (e.g. Basel Inkubator or Ecllosion in Switzerland).

### **Accelerators**

- Accelerators are organizations offering fixed-term, selection-based programs that include a range of support services and access to capital and investment in return for start-up equity. Accelerators that have commercial partnerships might not take equity (e.g. MassChallenge or BaseLaunch in Switzerland).

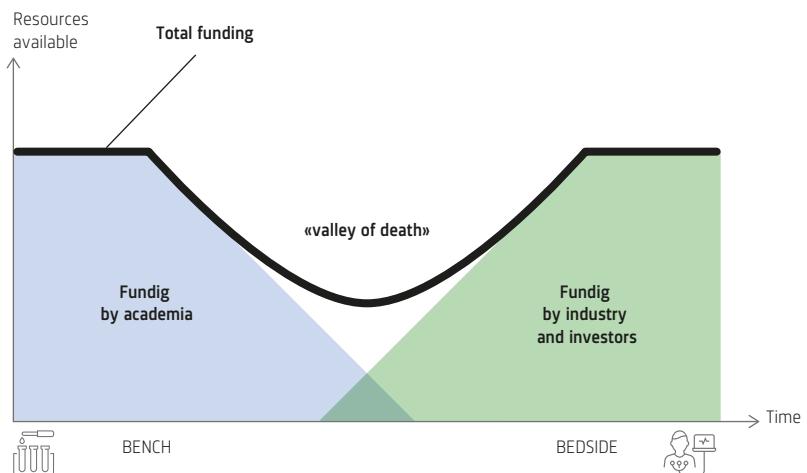
### **Technoparks and Life Science Campuses**

- Innovation parks host technology-driven public and private companies, and create an inspiring environment, with access to cutting-edge research, flexible and attractive real estate options, and a large network of dynamic entrepreneurs and established companies. Of note, an incubator can be located within an innovation park (e.g. Startlab in Biopôle, Table 2).

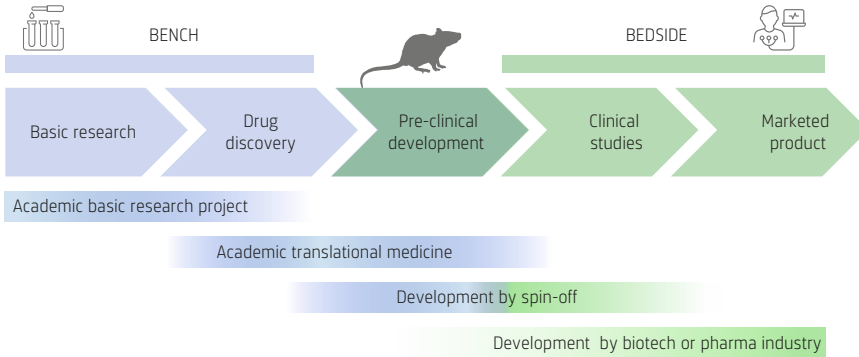
### Box 3: Valley of Death

The term «Valley of Death» is part of almost all presentations and media articles about translational medicine, and mainly describes a funding gap during the first part of translation, from bench discovery to first trials in human (usually between CHF 2M and CHF 10M), where no more basic research funding is available, and venture capital is not yet available. The «Valley of Death» often described in the Swiss media focuses on the need for larger funding (Series B and C, corresponding to CHF 5M to CHF >30M), where a gap is seen in Switzerland and where the risk for start-ups of moving abroad for this reason becomes bigger. In this context, some initiatives have been launched but still need to be implemented, such as the Swiss Future Fund or the Swiss Entrepreneurs Foundation.

By analogy, many use the term «Valley of Death» more broadly to describe the period between bench and bedside, where both funding and expertise in academia are missing. Butler describes it as the abyss left behind (by the pharmaceutical industry), where neither basic researchers, busy with discoveries, nor physicians, busy with patients, are keen to venture [1].

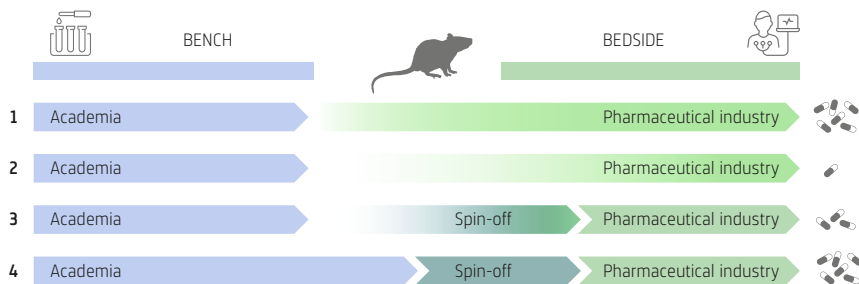


**Fig. 1:** Overview of the bench to bedside translational process



**Fig. 2:** The academia-industry continuum

1. A few decades ago (a sometimes idealized process), academia directly transferred its basic discoveries to the pharmaceutical industry for development and to bring them to the market.
2. Today, industry focuses mainly on de-risked projects, leaving a potential gap in the development of drugs of academic origin.
3. Spin-offs from academia can partially fill this gap, further developing promising academic projects if they have been developed sufficiently within academia to decide for incorporation and attract investors.
4. Academia should extend its participation to translation (despite gaps in knowledge, experience and expertise), to ensure that all promising projects are sufficiently developed to enable an informed decision on incorporation or out-licensing.





**Fig. 3:** Perception of academic and industry partners by each other**ACADEMIA**

## might think...

- They are only driven by money
- They have no understanding of science
- They are not that open to breakthrough innovation
- They are not able to reproduce my experiments
- Industry R&D is not flexible, cannot deviate from the plan
- They should not come too close to academia, otherwise they will corrupt or pollute academic research
- I will lose control over my research
- My patent will be stolen
- Contracting with industry will be long and complicated
- They will prevent me from publishing
- They can/will change their mind or focus at anytime for commercial reasons (or change in management) and stop project, even if successful

**ACADEMIA**

## should think...

- We can engage in a long-term relationship
- They can bring me expertise in development (clinical studies, pricing, reimbursement, etc.)
- We can learn from their structured R&D process
- We can profit from their network

**INDUSTRY**

## might think...

- They are unreliable (do not respect timelines, have no meaningful planning)
- They are dreamers with no sense of urgency
- They have no understanding of business and of industry standards (e.g. quality)
- Their experiments are not reproducible
- They are only interested in development of new knowledge, publication and education
- Their discovery process does not follow any plan
- Contracting with academia will be long and complicated
- They do not even have any animal proof-of-concept data
- Their new chemical entity or drug is poorly characterized
- We have no experience with their drug or technology
- They addressed a clinical indication that is known to be difficult (e.g. Alzheimer)
- They have an interesting therapeutic target but no drug that modifies its activity

**INDUSTRY**

## should think...






- They can bring in breakthrough science and interesting opportunities
- We can engage in a long-term relationship
- They might enrich our future pipeline
- They are flexible and can «follow the science», therefore innovate
- They will be future thought leaders for the therapy

**Table 1:** The main roadblocks to academic translational medicine

Rank	Identified roadblock	Average score (0–10)
1	<b>Gap between academic data and industry expectations</b> Gap between the scientific data that academic groups produce and what industry expects to engage in a partnership or consider in-licensing a technology.	6.9
2	<b>Lack of funding</b> Lack of funding for the projects, the people, the infrastructure, etc. during project development in the academic setting.	6.7
3	<b>Lack of academic resources to support project development</b> Lack of support by an academic structure that can provide guidance and coaching and help to move the project forward (e.g. by supporting project management).	5.9
4	<b>Lack of professional network to achieve successful partnerships</b> Lack of knowledge on which commercial or industrial partner to contact, when to contact them, what to ask, and how to find the right person in a given industry.	5.8
5	<b>Lack of education on translational medicine</b> The researchers are not well educated on the translational process. In particular, they do not have an overview of the whole translational process.	5.8
6	<b>Lack of expertise/knowledge in translational medicine</b> Researchers have little expertise or cannot easily access hands-on expertise in translation.	5.6
7	<b>Lack of academic culture for translation, e.g. incentives</b> The culture of translation is not fostered in academia. In particular, no incentives are offered to researchers.	5.5
8	<b>Lack of reproducibility of published data</b> Data generated by researchers cannot be reproduced by other groups, or more importantly, by industry.	4.9
9	<b>Lack of access to patients, patient data &amp; samples</b> Researchers have difficulties in obtaining access (often from clinicians) to the clinical database or patient population needed for their projects/clinical studies.	4.8
10	<b>Regulatory procedures too long/complicated</b> The process of obtaining authorizations from regulatory bodies (ethic committees, health authorities) to perform animal trials, clinical studies and/or obtain market authorization.	4.7
11	<b>Complex internal academic procedures</b> Procedures that need to be followed by academic researchers and that might slow down the execution of the project, for example compulsory public submission for outsourcing.	4.6
12	<b>Lack of national vision and structures</b> Absence of structure on the national level to coordinate the efforts in translational medicine.	4.6
13	<b>Time-consuming difficult contracts between academia and industry</b> For example licensing agreements or even confidentiality disclosure agreements.	4.5
14	<b>Lack of infrastructure</b> Lack of, for example, GMP or GLP facilities within academia.	4.5
15	<b>Lack of time</b> Researchers not having and not taking the necessary time to perform translational research.	4.5
16	<b>Suboptimal collaboration with technology transfer offices</b> Poor collaboration between the researchers and the future entrepreneurs with the technology transfer office of their academic center.	3.8
17	<b>Lack of political support</b> Lack of political support at the institutional, local, or national level.	3.1
18	<b>Lack of protection of inventions by academic inventors</b> Lack of protection of inventions by academic inventors, usually filing of a patent.	3.1
19	<b>Lack of motivation</b> Motivation of the researchers involved in a translational project.	2.9
20	<b>Lack of academic network</b> Local, national, and international network with other researchers.	2.5

GLP, good laboratory practice; GMP, good manufacturing practice.

**Table 2:** Institutions supporting translational projects in the top five Swiss universities and ETHs (non-exhaustive).

	Academic Drug Discovery Centers	Technology Transfer Office	Academic Translational Centers	Incubators	Accelerators	Innovation Parks & life science campuses	Associations and groups
 Zurich	DDNZ	Unitecra ETH transfer	TDA ieLab Wyss Zürich	-	-	Bio Technopark	
 Basel-Stadt	-	Unitecra	-	Basel Inkubator	Base-Launch	Innovation Park Basel	SCTD
 Berne	-	Unitecra	-	-	-	SITEM-Insel	Working Group for Academic Translational Medicine in Switzerland
 Vaud	-	PACTT EPFL office de transfert de technologies	Catalyze-4Life	Startlab	-	EPFL Innovation Park Biopôle	
 Geneva	-	Unitec	Accélérateur Translational	Eclosion Wyss Geneva	-	Campus Biotech	

**N.B.** There are many other centers in universities of applied sciences and in other cantons (such as the Swiss Integrative Center for Human Health in Fribourg or the MEDTECH Center in Lugano). DDNZ, Drug Discovery Network Zurich; EPFL, École Polytechnique Fédérale de Lausanne (Federal Technical University of Lausanne); ETHZ, Eidgenössische Technische Hochschule (Federal Technical University of Zurich); ieLab, Innovation and Entrepreneurship Lab; PACTT, Powering Academia-Industry Collaborations and Technology Transfer; SCTD, Swiss Center for Therapeutics Discovery; SITEM, Swiss Institute for Translational and Entrepreneurial Medicine; TDA, Therapy Development Accelerator.