How DanioLabs has evolved its relationship with the CIMR

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Abstract

The commonest interaction of industry with academia is as the passive recipient of intellectual property. A much deeper and productive interaction is possible with the creation of closely knit collaborations. Here the barriers to achieving this and how they may be overcome are explored.

INTRODUCTION

The majority of universities encourage the formation of spin-out companies. These spring forth from some, at least when the funding environment allows. One would therefore expect a close relationship to exist between emerging companies and universities, and by implication, academic scientists within the university. After the initial spin-out, further technology assets may need to be acquired and licensed from the university by the company. This relationship is often managed through the Technology Transfer Office (TTO).

One of the more complex relationships to manage between the spin-out company and the university is the one that involves any long-term collaborative agreement. Three players need to be aligned to ensure that any such collaboration is successful: the academic scientist, the TTO and the company, each likely to have a different view on the nature of the relationship and its measure of success. It is therefore not surprising that these relationships, if not carefully crafted and managed, can be fraught with difficulty. Consider for example what each party wants from such an agreement: the scientist often wants his/her work to be acknowledged as world-beating, to generate scientific publications and kudos; the TTO, wanting to ensure that some of the value is returned to the university; while for the company, the need is to own and protect any intellectual property, and ultimately to increase value to their shareholders.

The UK Government is keen to encourage productive technology transfer relationships through schemes such as the LINK and KTP (Knowledge Transfer Partnerships), but the dynamics still exist between the 'competing' parties. Key to a successful relationship, like all relationships, is the give and take in negotiations, a clear understanding of outcome, and an open and honest dialogue through the complete process, from initial discussions to completion of the last experiment and subsequent licensing agreements.

COMPANY BACKGROUND

DanioLabs is a therapeutics company that was founded in 2002 as a spin-out of the Department of Anatomy, University of Cambridge, following the completion of one of the founder's PhD. The university is an investor, and with previous representation on the Board, has always had a strong link with the company. The other initial investor was the Wellcome Trust, which was keen to encourage and facilitate interaction with universities in general.

A key part of DanioLabs' approach to drug discovery and development is the use of zebrafish to identify *in vivo* activities through the creation of validated disease models. Zebrafish are surprising amenable to disease modelling in larvae form as they are tiny, transparent vertebrates that have

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surprising human homology. Discovering therapeutics is more than disease modelling. No one company, not even the large multinational pharmaceutical giants, can expect to have full coverage of all technologies and expertise that may be relevant to the research and development process. Universities are an excellent source of research and development technologies, intellectual property as well as disease and therapeutic expertise that are invaluable to commercial organisations.

The most simple, but one-way, mechanism to access the universities' assets would be through consultancy agreements with key academics. Potentially more fruitful, but more complex, is the setting up of research collaborations where the flow of knowledge is more two-way. In this scenario, the competencies and skills of the academic group and the company are brought together, in order to identify where synergies may exist, where equipment, people and other resources maybe shared, and that data output from one group can flow into the other and vice versa. The most important output of such collaboration is the creation of new knowledge and intellectual property (IP). The desire for this sort of relationship formed the basis for the research programmes DanioLabs initiated with the university. Thus rather than being a straightforward IP exchange or transaction, it was the creation of a machine or enterprise to generate IP.

The proximity to Cambridge University offers an opportunity to integrate research capabilities not present in the Company

THE COLLABORATION WITH CAMBRIDGE UNIVERSITY

To date, DanioLabs' experience on the whole has been very positive in dealing with TTOs, with one or two exceptions. An example of our work with both the working scientist and a TTO is in the development of a major collaboration with the Cambridge Institute of Medical Research (CIMR), Cambridge University. Our relationship began through informal discussions pertaining to particular research questions, with one of the leading scientists in an area of commercial interest to us. These ideas evolved, culminating in several grant proposals, which were awarded to jointly to DanioLabs and the University.

A solid relationship was built slowly and initially informally, over several years

The fact that joint grants applications were successful, and that there was a cash element that flowed into the company from the joint awards, greatly facilitated the relationship. Still, the most important driver was the desire to create an integrated research group encompassing the traditional academic components of scientific endeavour with the translational and product development components of biotech. Some of the goals are the same, namely producing high-quality research – although with slightly different end-points in mind. For the academic, publication in high-quality peer-reviewed journals remains their primary currency, whereas for the company the added confidence in a product through the generation of high-quality data, and the higher price therefore attainable in its sale, are the key. Being able to move projects between the two institutions on a completely fluid basis was the goal. The lead investigators from both sides were in unison in wanting progress as fast as possible and for that to happen regardless of where the actual activity took place and, importantly with regards to IP ownership, by whom.

WHAT NEEDED TO BE CONSIDERED

Intellectual property

With these noble aims in place, what were the barriers in making this happen? Undoubtedly the biggest was how to handle IP issues, an area of concern to the TTO and the company, but also depending on the financial incentives agreed between them, the TTO and the scientist.

Understanding potential sources of IP, and to whom they belong, needs to be clarified. In addition, if the IP is owned by one party and that party wishes to acquire the IP, what is the process and licensing mechanism? For an early-stage

company that is likely to require further venture funding, the IP portfolio and rights it may have to the portfolio can be a crucial factor in fundraising.

Trust that both parties would take a sensible approach to IP in the future, was key

As part of the project involved early-stage work, there was not a single product that could be quantified, with the value agreed on prior to starting. Rather the project involved a lot of speculative work which might lead to something or nothing. It was felt important to avoid barriers to the free flow of information. Ad-hoc confidentiality agreements or material transfer agreements would have been difficult to work with. Additionally, the cost in implementing any one of these is comparatively high, both in terms of management time as well as downstream costs when documents are reviewed during due diligence exercises at subsequent investment rounds. This cost makes a lot of early-stage work and idea exchange between academia and commerce not practical as the activity needs to be worth at least a certain threshold value for it to be worthwhile to set up the various legal agreements. Having a much larger and broader collaboration enabled this to be overcome by having a generic agreement across the board. This generic approach needed the agreement of the TTO.

Lack of realism as to current market values can kill a collaboration

The next issue relates to how to agree future value. If the university is to get financial recompense for its input, and the company for their contribution, how does one agree how much input each party has made? Here to a large extent, it comes down to good working relationships, and a clear understanding of each party's needs. The fact that the founders had worked with the university for several years before and had developed a relationship with the TTO was key to getting buy-in. A working relationship among the three parties had developed, with a mutual understanding that the other was wanting only a fair proportion of value and would conclude any future agreements in a timely and sensible fashion. This was a key step in establishing the collaboration. This can be contrasted with an attempt at a smaller pilot project with another, much smaller, provincial university. Their TTO were, in our opinion, unreasonable in their expectations and demands, partly because of the inexperience of the TTO, with the result that, although DanioLabs would have liked to develop a research programme with one of the faculty members, the IP barriers put in the way by the TTO, and their expectation of future value, meant it did not attempt to take this forward. In our opinion, a TTO overestimating the value of long-term unproven IP is often the quickest way to kill any potential collaboration.

Staff contracts

With the agreement in place, the next problem related to practical issues of staff contracts. Some of our employees have their contract with the university, but work primarily at DanioLabs, whereas one employee is contracted through DanioLabs but works primarily in the university. The aim has always been to fully integrate all the staff into all company activities, so they are fully exposed to company culture and thought processes. The potential dangers therefore are that a university employee might contribute to a non-university project and claim ownership. This was overcome by making all the university employees working at DanioLabs consultants for areas outside their specific project. This meant that for all intents and purposes they could be treated equally.

Complete equality of academic and commercial staff maximises productivity of both groups

A thorough understanding of who owns what, and which party has the rights to intellectual property generated by their staff at different locations, is paramount. Ensuring that intra-project confidentiality is maintained through confidentiality agreements, and that relevant heath and safety procedures are adhered to can also be included in the consultancy agreements. The company and the academic investigator jointly interviewed potential candidates for the grant-supported posts.

Work culture

Company ethos is likely to be different from an academic one too, with much more structured and pressured working patterns being in place. The extent to which this is likely to cause a conflict is going to depend on the individual academic lab. A laissez-faire laboratory environment is going to cause more of a problem than a well-managed, highly driven group such as our collaborators at CIMR.

A win–win situation is eminently achievable

Financial tools

Accountancy issues such as how universities calculate costs, and how they will invoice, were further issues that needed to be resolved and should also be considered in any collaboration.

THE CURRENT SITUATION

Ultimately whether this will be worthwhile will depend on whether product identification and development have been accelerated. What has been found is that the university's input has a very positive effect with regard to experimental rigour, keeps the company's activities at the cutting edge and gives potential commercial partners increased comfort as to the quality of company activity. It has enabled the academic work to be more properly attuned to the realities of drug development, with certain activities having been abandoned and others prioritised. This has also enabled discoveries at DanioLabs to be explored further in an academic setting to increase the evidence of their utility.

RECOMMENDATIONS

In conclusion, our experience has shown us that one of the keys to a successful research collaboration is a recognition of the needs of each party to the agreement; the scientist, the TTO and the company. DanioLabs was fortunate in having already built a good working relationship with the academic scientist. This was an important step in ensuring that the three separate needs of the players could be aligned. There are a number of questions that need to be considered in working through the set-up of research collaboration, and some suggestions of these are given in Table 1. There is a need to be clear on outcomes, and the day-to-day relationship with the scientist. Sometimes having a good paper trail seems an overly arduous task, particularly if the initial relationship is built on mutual admiration, but it is important that it is agreed who owns what, what proportion of value will be apportioned to each group, and what happens if regrettably it

Table 1: Research collaboration matters to consider

Intellectual property	Who currently owns what?
	How could new inventions be created, by whom and where?
	Who owns new IP, and what are the criteria for ownership?
	What is the process for formal protection; who pays?
	How can the other party have access to the new IP and for what uses?
	What about IP that is outside the scope of the project?
Publications	Are these joint?
	Is there a mechanism to ensure that IP can be safe-guarded before publications?
	Can publication be blocked by a party?
Future value	How is it likely to be calculated?
	How is it to be split?
	Who can out-license and is there a timeframe?
	Under what conditions can another party take control?
Staffing	How will any new staff be selected and interviewed?
	Who do they work for?
	Are there provisions to ensure confidentiality outside the scope of the project?
Costs	How does each party calculate the costs of the project – what is included in any overheads?

all goes wrong. If such a relationship is to work it requires solid input from the principal investigators of each side and a commitment from both institutions. But once the academic/commercial research group is fully integrated and harmonised, the results are a very productive environment. The acid test is whether we would do it again, to which the answer is a resounding 'yes'.