Oxford GlycoSystems

Oxford University's first spin-off company

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One of the greatest changes in recent decades has been the way in which Government demands to see palpable and financially quantifiable results from science. Recent exchanges before the House of Commons Committee of Public Accounts show this well[1].

However, the two sides do not need to be in opposition. Despite the 'saloon bar wisdom' that every great British invention has been hijacked and exploited by others, there has been a history in this country of a smooth transition from pure science to practical application. Oxford GlycoSystems, the first spin-off from Oxford University in the field of glycobiology is a notable example of this in contrast with the American exploitation of such English discoveries as protein and DNA sequencing, and monoclonal antibodies.

Glycobiology

Glycobiology in Oxford grew out of my structural work on the antibody molecule. In looking at the effector functions of the antibody molecule which were mediated by receptors binding to the Fc region, we asked whether the conserved carbohydrates in Fc domain of the IgG molecule played an important role. This led to the challenge of studying the carbohydrate structures attached to the antibody. We set about establishing a unit in the early 1980s that could develop a systematic approach to analysing sugars.

Oxford University's first industrial grant

Funds were tight at the time so, with the help of Rodney Porter (who was Head of the Biochemistry Department), we decided to look to industry for support. Monsanto was one of the leading Biotechnology companies in the USA and in 1985 entered into an agreement with Oxford University to develop the technology for sequencing and releasing the sugars attached to proteins and also looking for their functions.

This was the first industrial grant in Oxford University's 950 year history. It was not without problems. There were people in Oxford who felt that the size of the initial grant from Monsanto (over £1m per annum) would "overbalance the University". There were questions raised as to whether it was actually right to accept industrial money. Monsanto, however, were sensitive to this and felt that they did not want to take advantage of Oxford in any way, and even offered to fund lawyers to represent the University against themselves! The final contract became a model for future interactions with industry. The grant was a 'Blue Skies' grant, but interacting with Monsanto taught Oxford the necessity of protecting intellectual property. This was really a new area for Oxford University, but we had a lot help from Monsanto. Indeed, Monsanto set an example in partnership by looking after the University's interests.

Glycobiology and academic discovery

By 1988, the word 'glycobiology' had been introduced into the language, I had become Professor and Director of the Oxford University Glycobiology Unit (later Institute), a Glycobiology course had been established in the Biochemistry Department, and Oxford University Press had started a journal called *Glycobiology*. With the build up of Personnel and Fellowships in Glycobiology, the first phase was complete (Figure 1).

Commercialization possibilities

The Monsanto grant attracted a great deal of publicity for Oxford worldwide. Sugars had become interesting. In Autumn 1986, I received a visit from three eminent US scientists from Harvard, MIT (Massachusetts Institute of Technology) and the pharmaceutical company Genzyme. They wanted to purchase oligosaccharides released from proteins using our technology and also the enzymes which were used to sequence them. They thought about expanding Genzyme's operations to include this. I talked to the officials in the University, and we registered a company called Oxford Oligosaccharides and considered whether we should sell the reagents.

Another first for Oxford University

Monsanto had acquired G.D. Searle by that time and the Searle officers were against commercializing the technology. I therefore agreed to take it no further, as my main interests were to preserve the research contract at Oxford. Searle were clearly impressed by this and suggested, by way of compensation, that they would be willing to fund and place up to 15 of their scientists in my group to help prepare the technology for commercialization. They then agreed that this could happen in a further 2 years: 1988. These scientists had dual reporting responsibilities to Searle and also to me at the University of Oxford. It was another experiment and another first for Oxford and it worked, because of the excellent quality of the scientists.

Figure 1. Universities are about knowledge, innovation and training; industry is about applications. Monsanto gave the University of Oxford a Blue Skies research contract in 1983. On the left are the academic outputs resulting from the Monsanto funding. G.D. Searle (which was part of Monsanto) also funded the Oxford Glycobiology Institute (OGBI) in 1991. A Searle Research Group was placed at Oxford University between 1985 and 1993, initially to help commercialize the technology for Oxford GlycoSystems (OGS), which was founded in 1988. OGS also developed technology mainly relating to proteomics and drugs, particularly Zavesca™ for Gaucher's disease which came from research work at the Institute.

The business plan

Meanwhile, the initial plan for business objectives and strategy was being compiled. My aim was to establish a world-class company, founded on the technology base represented in the Oxford/Monsanto research programmes. The initial objectives were to develop and market commercially viable products to serve the research and clinical community involved in carbohydrate-related research and diagnostics. Therapeutic applications of the technology developed by the programme would, however, remain in the province of Monsanto/Searle. The main products would be sugar standards, enzymes and instrumentation. The business model would also involve contract sequencing by way of validating the technology. Additionally, there would be a contract with Oxford University which would enable the technology to flow from my lab to the company.

Managing the different parties

There were still two trains of thought within Monsanto/Searle. The Monsanto personnel felt that Oxford Oligosaccharides should be given a very free range, since they were convinced that this would create the maximum opportunity to disseminate the technology and also to encourage others to work in it. In contrast, those in G.D. Searle were highly protective about leakage of technology. This was a constant tension which I had to deal with in the formation of the company. But I also had to deal with Oxford University, who had no experience in scientific start-up companies and to ensure there would be no conflicts of interest involving myself, my research and the company, a very important point in technology transfer, which is not always given sufficient consideration. To help in this, all my legal matters were dealt with by the University lawyer.

Venture capital

We started to write the rules of what the company could and couldn't do. The first rule was "The company must do nothing to bring the name of Oxford University into disrepute". Sir David Cooksey, the head of Advent in London and who had Monsanto/Searle's ear, met with the Vice Chancellor and other officials in the University, and legal documents were prepared. The initial investors were Advent Capital and Euro Ventures, two funds managed by Advent Ltd and Alafi

Figure 2. Development of automated carbohydrate release separation and sequencing. **(a)** The gel-permeation chromatography ('P4') system at the Oxford Glycobiology Institute, note heated water jackets, dual tritium and refractive index detectors, chart recorders and 1 m columns (1992). **(b)** Fraction collection for manual enzymatic sequencing. The output from the column shown in **(a)** is collected, and peaks are pooled and subjected to separate exoglycosidase digestion. This could take several months to complete (1992). **(c)** Left: GlycoPrep 1000, the first automated carbohydrate analysis system in the world developed by Oxford GlycoSystems from the technology of the Oxford Glycobiology Institute (1992). Right: RAAM (Reagent Array Analysis System) 2000 automated carbohydrate sequencer incorporating miniaturized column system with automated flow control, fluorescence-detection system and computer interface (1994).

Capital Corporation. Monsanto was a limited partner in each of these funds. I dealt with them separately and even persuaded them to compete against each other in terms of the initial price! The University, Monsanto, the scientists and staff were the initial shareholders, and a price was set for the funds to purchase shares.

A name change

The company was to be incorporated in the UK and was expected to have premises in the Oxford area. A Board of Directors was agreed, with representatives from the University, Monsanto and the investors. Licensing arrangements were to be put in place between Monsanto and Searle for the intellectual property from my research and also a Technology Agreement between Oxford University and the company. Headhunters were to be employed to find suitable CEOs. This was not going to be a 'nickel and dime' company and therefore we needed the best talent to make it work. Scientists had to be employed who understood the field, and the best choice was clearly my former D.Phil. student Raj Parekh, who was pursuing postdoctoral research in my group. It was decided that he would initially join the company for 1 or 2 days a week, but it soon became clear that the company needed him full-time to succeed. We changed the name to reflect that it was a technology company and Oxford GlycoSystems was born on 14 October 1988.

Although I remained as a Director of the company, the day-to-day running was firmly in the hands of Dale Pfost, an American who had a successful track record of developing scientific instruments. Within a year, the first products, biochemicals used in the analysis of sugars, were on the market. Oxford GlycoSystems was housed temporarily in Sir Martin Wood's start-up premises, but soon moved to its own new building in Abingdon. There the team was built up with engineers and scientists, with the idea of making accessible and automating the technology that had come from Oxford University.

The Glycobiology Institute

By this time, the collaborations between Oxford University and Searle on the drug front had also proved to be rewarding. Searle then funded the Glycobiology Institute in Oxford which was opened in 1991 and continued its support for the basic research programme at the University. In recognition that Glycobiology had emerged from the Immunochemistry programme initiated by Rodney Porter, the building housing the Institute was named the Rodney Porter Building.

Margaret Thatcher came to the Institute over the next 5 years. I was also summoned to Downing Street to see her on two occasions and once had a private meeting with her in Oxford. She told me how much she admired what we were doing, fundamental research in the University funded by industry, and having a spin-off company. She thought it could become a model for British science. She even discussed with me starting a new Glycobiology Institute somewhere else in the UK. However, I cautioned her against making this a general model, because I was aware that it would probably send the wrong message to British science and my colleagues at the university. I think she was offended by my answer!

Oxford GlycoSystems

Oxford GlycoSystems continued to grow and expand, and a number of automated machines such as the GlycoPrep 1000 (Figure 2) were produced, which were purchased by nearly every major pharmaceutical company throughout the world. There were tensions between the University and the company, as the scientists in the University were not involved in the engineering inventions which were necessary to commercialize and miniaturize the technology.

I attempted to get help in this aspect by appointing a Liaison Officer from Oxford GlycoSystems for the University, but it was difficult keeping all parties focused on the common mission at times. It was, however, very beneficial as members of my research team moved to work with Oxford GlycoSystems and their expertise and experience was invaluable and was, somewhat reluctantly at times, eventually recognized by the company.

Technology Development and Oxford GlycoSciences

Technology developed at a pace, and by about 1998, Oxford GlycoSystems had provided a large range of tools for glycobiology, and over 130 of its instruments for preparation analysis and sequencing of glycoprotein sugars had been sold worldwide. Additionally, technology development had continued with the introduction of a world-class automated proteomics platform. It was becoming clear to the company that it had all the tools for drug development. To reflect this, it changed its name to Oxford GlycoSciences — still OGS!

Late in 1998, the company was positioned to meet all the stringent requirements to float on the London Stock Exchange as a pharmaceutical company. One of its drugs, which was later to be approved worldwide, which was for Gaucher's disease, came directly from work at the Institute. In recognition of this, Oxford GlycoSciences announced grants of £1.5million to the Glycobiology Institute and, in addition, in a further collaboration, set up a 'state-of-the-art' proteomic facility in the Biochemistry Department, which is still functioning today. The close liaison with the University continued, sometimes with difficulties, but the clear success of the company was apparent to all. By the year 2000, the stock market value of the company had reach £1billion. In late 2002, the Oxford GlycoSciences drug for Gaucher's disease, Zavesca™ (Figure 3), received worldwide approval for therapeutic use.

It was clear that, to sustain that kind of growth, it was necessary to have a much larger portfolio of lead compounds. My own interests were now directed to the use of imino sugars as antivirals. I discussed the potential of this approach with Oxford GlycoSciences, but found that there was not a great deal of enthusiasm for entering the field of viruses, which was considered to be rather 'risky'. Undaunted by this, and driven by the research data in the Institute, I was determined to find an appropriate partner to develop this new class of antiviral drugs, and I was driven to seek interactions in the USA. In 2003, Oxford GlycoSciences was acquired by Celltech, which was itself later taken over by UBS.

Figure 3. Type 1 Gaucher's disease first oral therapy

Zavesca™ proved to be a very successful drug and today it is marketed by the Swiss company Actelion Pharmaceuticals Ltd. It is now being considered for use in other glycolipid storage diseases and in cystic fibrosis.

Oxford GlycoSciences remains an example of how technology could be spun off from the University and then spun back in to the University to help its technology programme and future research. It was undoubtedly a success, but it needed careful managing throughout. It was this element of managing and sensitivity that always provided challenges. ■

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