

Surviving in a 'knowledge market'

In the past 10 years, universities all over the world have come to realize that they are active in a 'knowledge market', which provides very attractive opportunities, but which is potentially also full of pitfalls. The fundamental and strategic research in the pharmaceutical sciences that is taking place in the universities is a clear example of a legitimate primary mission from which the pharmaceutical industry is the main beneficiary. This not only holds for the research results, but also for the training of highly skilled and motivated young scientists⁵.

Experience at LACDR

It is in this climate that in 1984 at Leiden University (The Netherlands) the Center for Bio-Pharmaceutical Sciences was established, replacing the former faculty of pharmacy. Its primary objective was to conduct multidisciplinary innovative pharmaceutical research, partially in collaboration with the pharmaceutical industry, and to offer a teaching programme to undergraduate, graduate and post-graduate students in the pharmaceutical sciences. In 1992, the Dutch Government started a campaign to advance and protect excellent research and graduate teaching by establishing inter-university research schools. The Center for Bio-Pharmaceutical Sciences at Leiden University merged with the Department of Pharmacology at the Vrije Universiteit Amsterdam, and the Leiden/Amsterdam Center for Drug Research (LACDR) came into existence. It comprises all the relevant disciplines for pharmaceutical R&D, from drug discovery and design to clinical drug research. For the latter purpose the Centre for Human Drug Research was

established, which is located in a purpose-built research facility in the Leiden Bio-Science Park. The staff of LACDR is composed of about 30 senior scientists, 30 postdoctoral scientists and 80 PhD students. About half of its funding comes in the form of a basic grant from the universities, while the other half is obtained from research funding organizations in the biomedical sciences and through collaboration with the pharmaceutical industry. Almost all the research groups have collaborative projects with companies, the most intensive being in the areas of molecular modelling/drug design, drug delivery and targeting, pharmacokinetic/pharmacodynamic relationships, and new bioanalytical strategies. Research is organized in interdisciplinary themes and results are reported in LACDR's Progress Report, published each year in April⁶.

LACDR has taken up the challenge of how a university can collaborate very fruitfully with an industrial partner without denying its primary mission of conducting high-quality research and offering a closely associated teaching programme. On the contrary, our experience is that the collaborations that have been developed with the international pharmaceutical industry are synergistic to this mission.

Douwe D. Breimer

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Controlling proliferation through collaboration

In this issue's Guest Editorial, Professor Douwe Breimer (Leiden/Amsterdam Center for Drug Research, The Netherlands) focuses on the increasingly valuable links between academic and industrial centres in discovery research. A unique illustration of this trend is provided by Prolifix, a young, pan-European company founded in 1994. The company focuses on the generation of new small-molecule drug leads, identified both through high-throughput screening and rational drug design, for the treatment of a range of proliferative diseases. The Prolifix operating centre is currently located at the UK's Medical Research Council (MRC) laboratories in Mill Hill, London, but is expected to move to separate premises within a year.

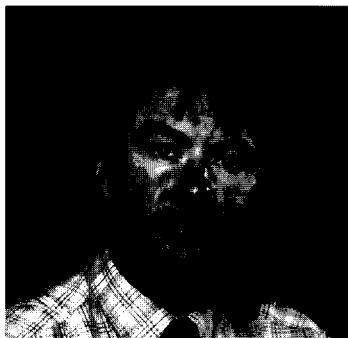
Therapeutic approaches

Prolifix coordinates several innovative programmes founded on control of the cell cycle. A primary focus is the control of diseases in which aberrant growth control contributes to the pathology. Prolifix aims to identify small-molecule therapeutic agents using a variety of approaches. The company has developed biochemical and yeast-based assays for screening chemical diversity libraries in order to find new leads that will act on critical growth regulating targets, such as E2F, a gene control protein, and thus control cell proliferation in tumours. A similar approach may also prove of value in controlling the hyperplasia associated with restenosis in occlusive vascular disease. Prolifix are also

capitalizing on an expertise in understanding the role of a critical cell-cycle regulatory protein in stimulating growth and division of breast tumour cells to develop novel leads that will control estrogen-receptor activity. In psoriasis, Prolifix scientists are focusing on M and S cell-cycle phases in the control of keratinocyte growth, and there is also an antiviral programme.

Establishing critical mass

The MRC has licensed to Prolifix intellectual property relating to targets, assay development and rational drug design, including the cancer cell technology of Professor Nick La Thangue (Prolifix's Chief Scientific Officer and Professor of Biochemistry, University of Glasgow, UK). However, although venture capitalists found the scientific and business concept attractive, according to La Thangue, "very early on, we got the clear message that we needed more breadth – more targets, more technology, more expertise in the company".



Professor Nick La Thangue, Chief Scientific Officer at Prolifix, and Professor of Biochemistry, University of Glasgow, UK.

Academic collaborations

In response, Prolifix have been able to identify the leading academic research centres in Europe and have established relationships that allow them to license-in the intellectual property of these expert teams. These arrangements include collaborations with Professor La Thangue's group at the University of Glasgow and Professor René Bernard (Netherlands Cancer Institute, Amsterdam), whose groups offered Prolifix complementarity with existing in-house expertise. Through this approach, Prolifix can access the expertise of around 60 academic scientists, whose responsibilities lie in overseeing the basic research programmes and providing input as members of the scientific advisory panel, for example in indicating where patents or inventions may be possible.

The result is an unusual organizational structure; the operating centre staffing remains very lean, consisting of the management and core scientific teams. The role of the centre itself is to act as a focal point for coordination of the research programmes and also to provide the central assay-building function and, in future, high-throughput screening resource. According to La Thangue, this paradigm enables the company to "access a lot of good technology, very quickly and effectively".

Rapid access

In consequence, La Thangue describes Prolifix, in essence, as "an assay-building,

high-throughput screening company" with access to a "web" of academic groups for very rapid access to technology and innovative cellular targets. As an example he cites the estrogen-receptor programme, a research area that has moved quickly in recent months and which has potential application for drug development in hormone-dependent cancer. Prolifix were able to access scientific understanding of the interaction between a cell-cycle regulating protein and the estrogen receptor, an association that affects the growth and development of tumour cells, before any work in this area had been published. They were then able to gain intellectual property that enabled them to discuss potential collaborations with major corporate players.

Industrial collaborations

At the same time, following negotiations with several large pharmaceutical companies, Prolifix established a deal with Japanese giant Chugai in late 1995. The deal will give Chugai access to the technology base of Prolifix and a 19.5% stake in the company in return for an up-front investment of £1 million and an ongoing funding programme. Prolifix are also entitled to a royalty on any drugs commercialized as a result of application of their technology. They have also been able to generate venture capital support from 3i (UK) and Atlas Venture (The Netherlands).

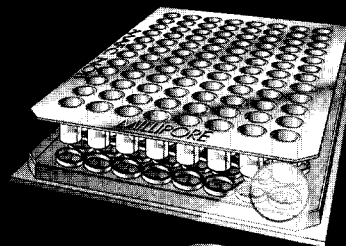
The future

The company perceives that its real strengths continue to lie in scientific input, affiliations with academic groups, intellectual property and know-how; "Intellectual property is very important, but so is understanding what to do with it", says La Thangue.

For now, Prolifix has acquired more intellectual property than it can actually use, so the company is not currently seeking to extend the academic 'web'. However, there is continuous dialogue with the academic world, and if an area is moving quickly in which Prolifix has an advantage, they will then seek to link up with an academic group. As La Thangue says, "more collaborations will happen".

David Hughes

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