



Photos (3): W. Koepfelle

Dealing with transfection near Strasbourg: the crew of Polyplus-transfection has 22 team members, including Managing Director Anne-Lise Monjanel (2nd from left) and CEO Joelle Bloch (5th from right).

Transferring nucleic acids in the Alsace: Polyplus-transfection (Illkirch/Strasbourg)

French Open

There are an impressive number of newly founded biotech firms in France, but most of them operate in splendid isolation. A severe lack of funding is worsening the situation. There are exceptions, however, in the Alsace.

A trip to the *Parc d'Innovation d'Illkirch*, located in the Rhine valley, a few kilometres south of the Alsatian capital, Strasbourg, is not to be taken lightly, particularly not on a cold and rainy March day. After bidding farewell to the talkative taxi driver who meandered about for a while and then charged 25 euros for a ten-minute ride from Strasbourg, one feels lonely in a moonscape-like no man's land. Several dozen futuristic examples of modern French architecture crowd barely two square kilometres, encircled by earthy fallow land, overgrown with scanty saplings and weeds. The streets are empty and once in a while a lone car drives by. It feels like the middle of nowhere.

It's hard to believe that there is life inside these spaceship-like buildings. But there is: Air France has a large base here, as well as Meteo France and lab equipment producer Fisher Bioblock Scientific. In addition, several state-run technology transfer and business development offices are located here. These include the *Ecole Supérieure de Biotechnologie de Strasbourg* (ESBS), which trains its students in Illkirch, as well as the IGBMC (a centre of biomedical research attached to the Louis Pasteur University, Strasbourg). Finally, dozens of French start-ups have made their home here.

Portholes in the Rhine valley

One of the youngest (and most unspectacular) buildings is a facility called Bioparc, established in 2004 and with corner windows that resemble portholes. In fact, Bioparc houses six young life science companies: Novalyst (a chemistry contract research firm), NMR-tec (which offers analytical services), Alix (a drug discovery firm),

Alsachim (synthesises isotope-labelled chemical compounds), Faust Pharmaceuticals (develops new drugs for neurological disorders) and Polyplus-transfection.

Behind the portholes, Anne-Lise Monjanel is sitting in her office and explains all about Polyplus-transfection. Monjanel was



The Bioparc facility, a recently constructed founder centre, located a few kilometers southern of Strasbourg, features futuristic architecture and confusing signposts.

involved in the company from the start. She is a co-founder of the five-years-old spin-off of the University of Strasbourg and is extremely well-travelled. As a student, she worked for a fragrance manufacturer in New York for two years and later lived in Nice and in Brittany. In 1989 she received a PhD in oceanography and decided afterwards to work as a teacher, which she did for nearly ten years. Today Monjanel works in biotechnology as Managing Director at Polyplus-transfection, meaning that she has to handle all marketing and sales.

The idea to found a company was born in an academic laboratory in Strasbourg in 2001, she explains. Jean-Paul Behr, a prominent expert in drug delivery and Research

Director at the National Center for Scientific Research (C.N.R.S.), had done pioneering work which led to nucleic acid carriers that were marketed by worldwide companies like Promega, Roche and Invitrogen. In January 2001, Behr decided to try his luck with his own company, dedicated to

the delivery of biomolecules. A quartet, consisting of him and Monjanel on the scientific side, and strengthened by the industrial managers Joelle Bloch (now CEO) and Patrick Metz (now managing director of a nearby Alsatian company) pooled their private funds of 349,600 francs (equal to 53,300 euros). With this money, they founded Polyplus-transfection. Nine months later, FCPI Avenir Finances, a seed venture capitalist firm from Lyon, contributed an additional cash injection of 600,000 euros (in 2004, Polyplus raised a further two million).

Beginning with 53,300 euros

Monjanel emphasises the relevance of industry-experienced people like Metz and Bloch. The latter, a former human relations manager and consultant, was at that time the only one who had the necessary knowledge and skills to supervise a company: "To have excellent scientific ideas like Jean-Paul Behr is one thing, but to manage a company is something completely different", she underlines. Two scientists, two businessmen and a touch of money – this *mélange* worked well, according to her: "We fit together very well."

Polyplus-transfection didn't make money from the very beginning, but it didn't take too long. The first product, a cationic polymer for gene delivery, had been proven successfully in the labs of Jean-Paul Behr, but, of course, there were no appropriately-sized solution containers, no packaging materials, no application-adapted protocols and, pivotal for a commercial company, not even a price-list. Thus, the small crew of less than a dozen people worked hard to develop the necessary product accessories, and after just five months, Polyplus' first product was launched under the name "jetPEI".

"PEI" stands for "polyethylenimin" (a branched, cationic polymerised molecule), which captures and protects DNA while forming positively charged particles that are incorporated by cells via endocytosis. After the DNA is released in the cytoplasm, it enters the nucleus, where the gene expression happens. The jetPEI reagent is a customised subtype of "ordinary" polyethylenimin, and according to the Polyplus 2007 catalogue, it achieves "a very effective gene expression with low residual toxicity and reproducible results". It is always difficult to verify such marketing phrases, but Anne-Lise Monjanel affirms that the first Polyplus

"All our first business took place in the lab of Jean-Paul Behr at the Université Louis Pasteur in Strasbourg."

product, for which Polyplus has an exclusive licence from the University of Strasbourg, is still her company's bestseller.

"The Bioparc of Illkirch didn't even exist at that time", Monjanel recalls, "all our first business took place in the laboratory of Jean-Paul Behr at the Université Louis Pasteur in Strasbourg". But in 2004, their rooms became too cramped. In a second round of financing, Polyplus raised an additional two million euros and was therefore able to move to Bioparc Illkirch and rent extensive premises. This sum doesn't seem very high, but it was sufficient for a tool development company like Polyplus. Monjanel takes the opportunity to underline the good relationship between Polyplus and its investors. They don't expect fast and financially-driven growth but an organic development of the business, she says.

Polyplus is owned not only by the founders and investors but also by its first three

employees, who obtained shares in the company. The current shareholders don't want to lose control of their investment, Monjanel adds, and for this reason she is sure they have no intention to go for an initial public offering (IPO). In addition, the conditions for an IPO are not particularly favourable in France.



Joelle Bloch (left), now CEO, and Anne-Lise Monjanel (right), now Managing Director, founded Polyplus-transfection in 2001.

In 2006, a total of 22 employees produced a turnover of 1.5 million euros. For this year, Monjanel expects a 25 percent increase, reaching two million euros. By her own estimations, Polyplus will re-invest 60 percent of its revenues in research and development. The company isn't making a profit yet, but should break even at the end of 2007. Polyplus makes 50 percent of its sales in Europe. Normally, one would expect the other half to take place in the USA but, surprisingly, Polyplus-transfection has a strong foothold in the Asian market and sells its transfection kits in great quantities to countries like India, Japan, South Korea and Taiwan.

A strong foothold in the Asian market, and a crucial office in the USA

To strengthen its commercial operations in the USA, Polyplus has established a regional office overseas. "The reason is that some of our main competitors are domiciled in the United States", says Monjanel, who names Invitrogen (as the most important), Stratagene and Mirus as examples, not forgetting Roche Diagnostics of Switzerland and Qiagen from Germany.

Wherever the parcels leaving Illkirch are posted, the address always includes the name of a research department, either of a university or of a life science company. Polyplus produces a glossy 44-page cata-

logue about its 20 products. Big names order the small Alsatian company's transfection agents, including Novartis and Pfizer (mostly via local distributors) and – believe it or not – their competitor, Roche. Besides its "big hit" jetPEI for the delivery of nucleic acids, Polyplus offers also "PULSin" for the delivery of proteins, antibodies and pep-

tides into living cells. Recently, the firm completed its line up with the development of the novel *in-vitro* reagent "INTERFERin", which delivers siRNA into cells.

The French entrepreneurs have even ventured out into the big wide world of drug development. In a cooperative project with a team of researchers from the Hebrew University of Jerusalem under Avraham Hochberg, the transfection reagent jetPEI was used to introduce a toxic gene into bladder cancer cells. In June 2004, the Israelis published their results, attesting that the tumour's size had reduced by more than 75 percent and that the cancerous cells had almost stopped growing. Now the Israeli scientists are working on further gene therapy experiments.

Good reasons for staying in Alsace

For those who have developed an appetite for small Alsatian companies like Polyplus after reading this story, Monjanel gives the following advice: "Job applicants have to be young and open, must be able to provide an university degree and speak the English language fluently." Fulfilling the latter criterion is not easy, she adds, not even in the modern France of 2007. "To find good scientists in the Alsace", however, is easier, "because the University of Strasbourg has a very good reputation."

And the long distance to Paris, the commanding and centralised capital of France? Is it a handicap to be located in Alsace? Monjanel thinks not. She cannot name a single disadvantage and is enthusiastic about the good biotech network in the Biovalley, a cross-border biotech region which encompasses Basle, Freiburg and Strasbourg and comprises 300 life sciences companies, the pharmaceutical companies Roche, Novartis and Aventis and four universities with 70,000 students.

This sounds good to Swiss and German ears since the southeastern part of the Biovalley often worries that their French counterparts are rather too insular.

WINFRIED KOEPELLE