



Photo: R. Florés

Doing business in the 'biotechnological desert' of southern Spain: Biomedal's team with founder and chief executive officer Angel Cebolla (4th from left).

Tools for Protein Processing in Spain: Biomedal (Seville)

Mediterranean Sundance

Seville, capital of Andalusia, is the cultural and financial centre of southern Spain and a tourist hotspot. Biotechnology isn't something one would expect to find here. But appearances can be deceptive...

“It was not just making money. Among my motivations in creating the company was also a good portion of idealism... the will to change things.” Angel Cebolla is Chief Executive Officer of Biomedal, a biotech company located in Seville, Spain. He is a friendly person that hides, under his shy, ordinary appearance, a handful of strongly held moral convictions and something approaching civic rebelliousness. These hidden qualities strengthened his resolve when facing the ultimate challenge: the creation from nothing of a biotech company in the biotechnological desert of Southern Spain ten years ago.

Although Biomedal is still a relatively modest company it already satisfies many of Angel's goals: independence, initiative, creativity and the ability to generate wealth and employment. “I believe this is also a kind of altruism” says Angel timidly. This, briefly, is his story.

Nothing unusual at first

There was nothing unusual about Angel's scientific career, which followed the same pattern of many other young Spanish scientists. After getting a PhD in microbiology at the University of Seville, he began his postdoctoral peregrination. First he went to the Centro Nacional de Biotecnología in Madrid, where he continued his microbiological research in depth. Later, he moved to Gif sur Yvette, France, where he learned about plant molecular biology at the Institut des Sciences du Végétal.

Whilst a postdoc he twice applied for a position in Spanish public research. Both times he was rejected in favour of candidates with fewer objective merits. For Angel, this was a formative experience, sharpened by his belief that the evaluation process had been unfair. At the time (about ten years ago) new positions for scientists in Spain were scarce. And, although nepotism was rife expressions of public indignation were rare and most people resigned themselves to accepting the system as it was. Many postdocs that were abroad and willing to return



Photo: Consorcio Turismo Sevilla

The famous royal Alcázar Palace in Seville, one of the best remaining examples of mudéjar architecture, built over Moorish ruins in the 14th century.

to Spain felt frustrated and hopeless. During the summer of 1997, some of them, including Angel, found release in the form of a discussion forum about science and politics held online by *El País digital*. A group of Spanish postdocs with similar concerns met on the forum and began to share their opinions and problems. “That was very exciting”, says Angel. “We might be scattered all over the world but suddenly, thanks to the Internet, we were not alone”. Following Angel's initiative, they decided to stop complaining and to work together for the benefit of Spanish postdocs and science. This is how they founded the Association for the Advancement of the Spanish Science and Technology (AACTE). Since then, this association has fought against endogamy and nepotism at universities and played an active and critical role in forming Spanish scientific policy.

“I guess I had a natural disposition towards business. I had always liked making numbers and estimating in my mind the financial possibilities of businesses that I saw around me or that I simply invented,” says Angel. “On the other hand, I disliked the ri-

gidity of the functionary system and did not even want to think that I had to play that nasty game of patronage if I wanted to return to Spain. But there were no other options for a young scientist. It was in France when I began to consider that creating my own biotechnological company could be a serious alternative.”

His own company as an alternative

A Marie Curie Actions grant gave him the opportunity to return to Seville, where he found a dynamic and open-minded research group that agreed to support his projects. Resolved to give his new research a definite biotechnological character, he began exploring the commercial possibilities of certain expression vectors that he had designed when working in Madrid. His first reward came when the American biotech company Active Motif requested the license for some products that Angel and co-workers had presented at a biotechnological fair. Angel was beginning to speak the business language more fluently. Meanwhile, he began to collaborate from the university with various Span-

ish biotech companies and to attend courses on business management and marketing. Angel took strength from meeting other enterprising colleagues with similar concerns. Together, they decided to present a business plan to a project competition dedicated to boosting the enterprise and economic development of Southern Spain. Angel and colleagues won one each of the 'best business idea' and the 'best business plan' prizes in the field of biotechnology and, with the technical and financial help of the foundation's experts, created Biomedal in 2000.

The "family & friends" programme

They began with about €20,000, just enough to set up a modest office and a sketchy lab, and to buy some bubbly for the inauguration party. Later, they got more money from "family, fools and friends" and bank loans. The all-important public funding would come later, in the form of projects and other awards. Once the company was up and running, it split in two: Angel's partners focused their interest on human genetics and created a new firm called Neocodex. Angel took on the leadership of what remained of Biomedal and backed the development of research and diagnostic tools.

"An essential attribute you need to be able to undertake such a risk is self confidence," says Angel. "You need to believe that you are able to do it. And this is not always easy. Somehow we are educated to behave like sheep in a herd, and the promotion of essential values like self-esteem, independence or creativity is neglected. I was not immune to that atmosphere. I gained my self-confidence progressively during my scientific career, as I could satisfacto-

rily solve the successive research projects in which I got engaged. Also the experience with the AACTE was very revealing. It showed me that you should always try to change what you don't like, better than just waiting passively or resigning yourself."



Photo: Florés

"Self confidence as an essential attribute":
Biomedal's founder Angel Cebolla in his office.

In Angel's opinion, the main constraint on the biotechnological development of Southern Spain is not a lack of talent or knowledge, but a lack of initiative. "We have an inferiority complex that handicaps us. I had to go abroad (during my postdoc stage) and meet people who were doing outstanding work to notice that they weren't a different species, but just ordinary people, like you and me. Some technical experts I met in certain biotech companies in the USA used to have higher salaries and a lower scientific background than many of my university colleagues in Seville... There is a lot of cheap talent in our universities, but the Spanish functionary system suppresses most of the potential that they could offer society."

Biomedal is already six and a half years old, still going strong and growing healthily. Although 50% of the company still re-

lies on public funds, invoicing has grown on average by more than 30% per year. Today, Biomedal boasts 15 employees, eight patent licenses, a catalogue containing more than 100 products, clients all over the world and distributors as far afield as China, India, Japan and Italy. It participates in several Spanish and European research and development projects and is a partner of Ingeniatics Tecnologías, another new company from Seville that exploits a technological platform for fluid manipulation at micro- and nano-scale. And, of course, they have copious plans for the future. This year they aim to launch a new series of products with the support of outstanding scientists from Stanford University, and to incorporate novel diagnostic tools into their catalogue.

Main focus on the Spanish scene

Although obliged to confront tough global competition, Angel thinks that small companies can find their own niche and that in certain conditions they can be more competitive than big multinationals. "Like ants that feed from what giants discard" he remarks.

Although open to ideas from anywhere, their aim is to focus mainly on Spanish scientific production. "Spanish science is growing up. The pity is that most of our scientists that do basic research usually show very little interest in looking for the applied side of their findings. Papers are usually much more appreciated than patents. But patents are the first steps for society to recover part of its investment in science. Our scientific production is increasing and getting better and we have to be ready to take advantage of it."

RAFAEL FLORÉS

Spanish Biotech Companies

Southern Selection

According to the European Association for Bioindustries (EuropaBio), Spain has 81 biotech companies (other sources list as few as 57 or 71). In any case, the biotech sector is noticeably underdeveloped when compared with huge European biotech nations like Germany and the United Kingdom, boasting some 500 biotech firms each. In the following, we introduce six upcoming newbies and an established old war-horse, located in Madrid, Barcelona and Seville.

Advancell (Barcelona) was founded in 2001 and develops *in vitro* cell models as research services at its three operational sites in Barcelona, Valencia and Galicia.

Biomedal (Seville; see story above) was founded in 2000. The company is focused on the production and purification of recombinant proteins and the metabolic engineering of microorganisms. Biomedal develops new procedures and both molecular and cellular tools for research, diagnostics, production and purification of biological material. Biomedal also handles consulting and technology transfer contracts. The Sevillian's main product is a bacterial protein expression system that provides high-level expression.

Crystax Pharmaceuticals (Barcelona) is a privately-owned drug discovery company. It was founded in 2002 as a spin-off of the Span-



Biotechnology in Spain

Still a Lot to Be Done

There's good news and bad news when it comes to Spanish biotechnology.

The good news is that the Spanish biotech sector has enjoyed a growth rate of 350% over the last four years.

The bad news is that it faces a severe lack of funding and conservative, repressive laws.

Spain boasts one of the biggest global economies. With an impressive gross domestic product of \$1,126 billion in 2005 it ranks 9th in the world. When it comes to biotechnology, however, Spain is positively dwarf-like – even in Europe, where much smaller countries such as Sweden, Switzerland and Denmark are light years ahead. According to estimates, Spain, with its population of 40 million, has only 81 pure biotech companies, employing a total of 2,200 people (all figures taken from *Biotechnology in Europe: 2006 Comparative Study*, The European Association for Bioindustries). The three smaller nations mentioned above with populations of barely 30 million apiece have 379 biotech companies, employing more than 25,000 people. In other words, countries like Denmark and Sweden have a 15-fold higher number of biotech jobs per head of population than Spain.

Biotechnological peanuts

In a 2005 list of the world's top 100 biotechnology companies, ranked by revenue, 20 firms came from European countries (including seven from the UK and three

each from Switzerland, Germany and Sweden) and 66 came from the USA. The list included no Spanish companies at all. Unsurprising when you consider that the typical Spanish biotech was founded few years ago, has a fistful of employees, doesn't produce noteworthy revenues (usually less than €1million) and is in the red for years.

The Spanish biotechnology sector achieved revenues of only €260 million in 2004, barely 1.2% of the European total of €21.6 billion. Moreover, the Spanish venture capital scene is underdeveloped. Annually, less than 1% of total biotech venture capital raised in Europe ends up in Spain (rather underwhelming when you remember that the country is home to more than 8% of the EU's population).

A glimmer of hope

A desperate situation? Granted. But there is hope. The number of Spanish biotech start-ups has skyrocketed in recent years. Nearly half of the 81 companies mentioned above were founded between 2002 and 2004 (more recent data are unavailable). Spain resembles Germany ten years ago. There is a lot of optimistic

founder spirit and thousands of young researchers coming up with good ideas, but the necessary venture capital is missing, along with supportive legislation. Moreover, the Spanish are conservative and tend to invest in other business areas. It's time to change their minds. W. KOEPELLE

Don Quixote and Sancho Panza (at the Miguel de Cervantes memorial in Spain's capital, Madrid).



ish National Science Council (CSIC) and the Technical University of Catalonia by a group of experienced scientists. Crystax provides protein crystallography services, high-throughput NMR and fragment screening for structure-based drug discovery.

Era Biotech (Barcelona), founded in 2002, employs 12 people and develops cell-based biomanufacturing technologies for boosting production of recombinant proteins in plants and cultured cells.

Oryzon Genomics (Barcelona) was launched in 2001 as a spin-off of the Spanish National Research Council (CSIC) and the University of Barcelona. The company identifies the relationships between genes and functions focused on cereal agrogenomics as a genomic and biotechnology service to industry, hospitals and public research centres. Specialising in plant genomics, Oryzon has a staff of 30 scientists.

Puleva Biotech (Madrid), founded in 2000, is part of the Ebro-Puleva group, Spain's largest agro-food business. It develops and commercialises food in the field of "functional nutrition". In 2005 the company had 49 employees and turned over 7.1 million euros.

Zeltia (Madrid), a colourful mixture comprising half a dozen junior enterprises, is the heavyweight amongst Spain's biotechnology companies. The parent company, Zeltia, calls itself a "world leader in the discovery and development of drugs of marine origin" (a more or less meaningless phrase). Zeltia's scope is broad: Pharmamar, the best-known subsidiary, specialises in the discovery of new cancer drugs, whereas Neuropharma seeks novel treatments for neuro-degenerative diseases. Genomica is developing molecular diagnostics tests and Zelnova produces chemical compounds such as insecticides and rat poison. In 2005, Zeltia's total revenue fell to 72 million euros. -WK-