ANDALUSIA, SPAIN

## Growing citrus and cell lines in southern Spain

Famous for its orange groves and flamenco dancing, Andalusia hopes to find prosperity in science and technology, with a focus on biomedicine.

"To me, Andalusia feels TALK TO any veteran research a bit like California in the 1960s." José Miguel Ramil, CITRE

administrator in the Spanish region of Andalusia and the first thing they will point out is the transformation of their professional lives. The changes have come through a new driving force underlying the region's economy. The predominant image of Andalusia has long been that of a region heavily reliant on tourism and farming, with deeply rooted cultural traditions. But for the last 20 years, particularly the past decade, research investors at all levels — from the European Union to Spain's national and regional governments — have grasped the region's potential as a centre for excellence in research and invested accordingly. The biomedical sector stands out. Andalusia is the second of Spain's 16 autonomous regions when it comes to biomedicine, according to the Organisation for Economic Cooperation and Development (OECD), and the region accounts for 19% of the sector's total corporate presence in Spain. One scientist who has watched

the trajectory is José López-Barneo, a professor of physiology at the

Cordoba Seville • Andalusia Granada University of Seville's medical school. He also heads the Seville Institute of Biomedicine (IBIS), one of a small collection of new research institutes in Andalusia. IBIS has been on the map since 2006, but only recently moved into a custom-built facility at Virgen del Rocío University Hospital in Seville. "If we compare ourselves to how things used to be, the change has been very big," he says. "The number of investigators and groups that are doing research at an internationally competitive level has increased significantly."

One of the main drivers of Andalusia's scientific expansion has been the European Union's Lisbon Strategy, which set strategies for economic development across the EU between 2000 and 2010. Andalusia was identified as a priority area for development and was allocated €6.8 billion from the European Regional Development Fund (ERDF) between 2007 and 2013 to boost economic growth and employment opportunities. The region's government, Junta de Andalucía, has created several formal programmes for distribution of this funding and its tax revenues over the six years, including programmes called PIMA and PAIDI that are designed to promote innovation. PIMA has a budget of €5.7 billion, of which €2.7 billion is earmarked for encouraging knowledge-based industries, while PAIDI promotes biotechnology, bioengineering, health sciences and nanotechnology as areas where government expenditure is most warranted.

The appearance of green shoots is proof that such programmes are nurturing economic growth. One such indicator is the decision of CITRE, the technology transfer arm of multinational pharmaceutical company Celgene, to site its European office in Seville. "The decision [to go to Andalusia] took about a year," explains CITRE chief executive José Miguel Ramil. "We were looking at different options: at the size of the region, the quality and the integrity of the health system, the reputation of the universities and how easily we could collaborate." After careful consideration, CITRE decided that Andalusia provided the most complete package. "To me, Andalusia feels a bit like California in the 1960s," says Ramil, referring to the US state's rapid industrial expansion at that time. "The government here is really trying to change the basic structure of the economy."

#### California dreamin'

Like in California, Andalusians enjoy surfing spots, vineyards and orange groves, but the region also has a public health system that is particularly conducive to research. Owned and run by Junta de Andalucía, all patient records are electronic and integrated in a shared data management system that makes it easy for investigators to identify patients who may wish to take part in clinical trials. IBIS's Barneo, who is also director of research at Virgen del Rocío University Hospital, says such access enables scientists to find unusual case studies as subjects for basic research. "You can imagine any kind of rare disease that you want to investigate and if you are having trouble locating samples, you will find them in my hospital," he says. "Andalusia has a very decent public health system, from the point of view of teaching and seeing patients. It's also well organised and there is very close contact between universities and hospitals."

Most research within Andalusia's public health system is coordinated >>>

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by the Foundation of Progress and Health (Fundación Progreso y Salud, or FPS), which Barneo says has a good understanding of the complexities involved with research management. "To do really good work, the institutes have to be independent from the point of view of management while also being able to closely interact with the health system," he says. "The management [of the whole system] needs to be very sophisticated to have universal health care that is compatible with making our institutions attractive to the best human capital in the world."

The benefits of doing research within the public health system are recognised beyond Seville. José Antonio Lorente, who runs Genyo, a genomic oncology research centre — based in Granada and set up by Pfizer, the Junta de Andalucía and the University of Granada in 2010 — says he is proud of what Andalusia can offer biomedical researchers. "We're all inside the same network [so] we have immediate access to up-to-date information from all other research groups," he says. In Genyo's short history, the network provided by FPS has been a conduit for collaborations with several of Andalusia's universities, including informal partnerships between laboratories and formal agreements at the whole-institute level. It has also been a starting point for joint projects with private companies. Lorente plans to extend Genyo's collaborations further to include investigators in the region's hospitals and primary care doctors.

Such a straightforward means of identifying synergies might



CABD (Andalusian Centre for Developmental Biology) is expanding its vertebrate research.

explain why research funding in Andalusia generates a lot of output. Of Spain's autonomous regions, only Madrid and Catalonia published more research papers than Andalusia between 2003 and 2008, according to research group SCImago, and they both spend significantly more on research and development as a proportion of gross domestic product.

#### **Biomedical hopes**

As with IBIS, the majority of new research institutes in Andalusia focus on biomedical research. CABIMER (the Andalusian Centre for Molecular Biology and Regenerative Medicine) and CABD (Andalusian Centre for Developmental Biology) opened in Seville in 2006 and 2003 respectively, and IMIBIC (the Maimonides Institute for Biomedical Research) opened in the smaller city of Cordoba in 2008.

CABIMER is divided into four departments — two focus on basic molecular research and two concentrate on more clinical areas. In the first category is the department of molecular biology, headed by Andrés Aguilera. He's particularly excited about his group's research on the cellular machinery that corrects double-stranded DNA breaks. Recent discoveries include the finding that a gene involved in some neurological disorders also plays a role in genome integrity, and that mutations in a group of genes involved in messenger RNA production and genome integrity halt the development of model organisms once they reach a certain threshold. After five years in his role, Aguilera is happy with progress at CABIMER. "One of the strengths of the centre is attracting good young researchers. One just got a European Research Council starting grant," he says. "That's means we're doing a good job of selecting people."

CABIMER's other departments are also breaking ground, focusing for example on apoptosis and how material enters and leaves the cell's Golgi apparatus. "Some of the groups have developed stem cell lines that might be useful for the future," Aguilera adds, explaining that the centre has a strong interest in exploring the potential of stem cells as a treatment for diabetes. Stem cell research is also being



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supported at a regional level and, in 2010, the Andalusian Initiative for Advanced Therapies signed a collaboration agreement with US stem cell research centre, the California Institute for Regenerative Medicine (CIRM). The agreement, one of 11 international funding collaborations established by the CIRM, will make it easier for researchers in Andalusia and California to obtain joint funding and share knowledge.

CABD also has an international outlook. It was formed when Spanish developmental biologists working in laboratories around the world came together. The institute was the brainchild of renowned scientist Antonio García-Bellido, who wanted to further Spain's strong tradition in developmental biology, and his colleagues. García-Bellido discovered how to monitor the development of Drosophila embryos and found that HOX genes (which stipulate the development of different body parts in all animals) are controlled in a compartmental way. CABD researcher James Castelli-Gair Hombría, who studies how HOX genes control morphogenesis, says the centre is particularly focused on expanding its vertebrate research: "We have a very big zebrafish facility that does a lot of work on genome regulation, and we are also getting some mouse researchers."

IMIBIC is also taking on new people. To keep its work current, the 30 research groups that comprise IMIBIC take on at least 25 new researchers between them each year, via internal and external recruitment. Since it was founded in 2008 through an agreement between the Andalusian public health system, the University of Cordoba and Queen Sofia University Hospital, IMIBIC has worked on a range of projects with Tufts University in the United States and with researchers in Germany, England and Spain. Its scientific director, Francisco Pérez Jiménez, tells of his major project, a clinial trial that will monitor 1,000 people with cardiovascular disease over five years. "We are trying to demonstrate that a Mediterranean diet with lots of olive oil is better at preventing a second heart attack than the low-fat, high-carb diet that nutritionists currently recommend," he says. "We have a really important advantage in our environment because we have experimental researchers in basic science and also clinical researchers."

#### **Future of funding**

While researchers in Andalusia are concerned about Spain's experience of the global financial crisis, most are sanguine about the future of their own research budgets. The national government has kept its promise to retain the funding of internationally competitive science and as a result, despite some uncertainty over how Andalusia will spend its budget after 2013, both Genyo and CITRE are planning to expand their operations. Considering the energy surrounding these institutions, the field of biomedical research looks poised to provide the economic spur for Andalusia that the regional government is aiming for. Nature editorial staff have no responsibility for content

AMES CASTELLI-GAIR HOMBRÍA

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