



## Editor in the field Madrid's CNIO

It takes many mutational steps for a cell to become a cancer. Each step makes a distinct contribution to the independence of the cell until the cells collectively overwhelm

the body. Fighting fire with fire, Mariano Barbacid established the Centro Nacional de Investigaciones Oncológicas (CNIO) by assembling researchers from all over the world. Each has contributed crucial insights into one or more of these steps. He had an advantage: they happened to be Spanish, and they were happy to come home.

Some of these steps are large enough to be considered milestones. The discoveries of the dominant V12 mutated Ras oncogene, the p16 tumor suppressor and telomerase receive a great amount of attention in the cancer field in large part because of research by the investigators now forming the nucleus of the CNIO: Barbacid himself, Manuel Serrano and Maria Blasco. Between the milestones lie routes, cancer processes linking the mutational steps, processes where Spanish researchers were again able to make distinctive contributions. This has been most notable in areas such as DNA methylation and histone modification, studied by Manel Esteller, and genome instability, which preoccupies Oscar Fernández-Capetillo. In the signaling mechanisms they use, cancer cells reveal a lot about themselves and their relationship to normal cells, particularly in the signaling cascades of protein kinases, tackled by Ángel Nebreda and Marcos Malumbres. But CNIO is not just for the Spanish; this institution is looking to attract and train cancer researchers from all over the world.

Traditionally, Spain has not invested a large proportion of its gross national product in research. For example, research grants in Spain are not currently designed to support the expenses of running a building. Despite this, the country seems to be an increasingly attractive place to work in some strategic areas, including biomedical research. For example, the Socialist government of Spain is one of only four in the European Union (EU) that currently approve human embryonic stem cell research. Regardless of government, it has been possible to establish truly autonomous and competitive research institutes in Madrid and Barcelona, and this has entailed a break with traditional career and funding structures for science. CNIO is directly funded by the Spanish Ministry of Health, rather than by the government's research councils, for two thirds of its budget, giving it a unique management system for Spain (now replicated in Barcelona). The principal investigators are not civil servants and receive indefinite

contracts. The director has full budget control and ability to hire worldwide, subject to EU employment law. The current CNIO staff of ~300 is expected to expand to 500.

Construction of the new CNIO building was started in 1999 and finished in 2002. It is fair to say that the building floats on a substantial infrastructure of mice, meetings and biotechnology. Mouse models that closely reflect human cancers are one key part of the overall research strategy that concentrates on molecular diagnosis and drug discovery. From the *Nature Genetics* perspective, mouse models are poised to become very important indeed. Many of these have been developed at CNIO, the Netherlands Cancer Institute and others. But despite considerable efforts by the researchers and the member states, it is unclear whether the rather mysterious and unresponsive EU Framework funding model will be able to secure the European advantage in this area, faced with the excellent organization of competitors like the US National Cancer Institute's Mouse Models of Human Cancer Consortium.

Drawing on his many years of research both at the National Cancer Institute and at Bristol Myers-Squibb, Barbacid concludes, "the time is right for academic institutions to do drug discovery without the pressures of industry and the pharmaceutical companies." Two unrelated groups funded by Eli Lilly currently cohabit the building, making use of the new facilities and helping to pay the rent. No teaching hospital is associated with the institute, but that is perhaps a virtue, as Madrid is a city of six million people, and thousands of tumor samples from the entire catchment find their way to the tissue banks of CNIO. Collaborators who can make use of this resource are eagerly being sought. The core biotechnology staff of 70 serves the whole institute, designing and analyzing microarrays on various platforms. The genetics group has recently added a high-throughput SNP genotyping facility under supervision of Ana Gonzalez-Neira.

The design of the library, public spaces and labs reflects a group of researchers whose science is driven more by enthusiasm than by routine. For example, the director is only half joking when he says that the interlock portal to the animal facility had to be absolutely "Spaniard-proof." Madrid is the perfect city for researchers who have not yet realized they might need to sleep and whose idea of a balanced life is amid opposing rip currents of scientific and cultural passions. The team Real Madrid no longer trains across the road from the institute, now that they have a monumental soccer city out by the airport. Still, they play at the legendary Santiago Bernabéu stadium, only three subway stops from the CNIO. ■