

Foreword



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Director

2010 has been a transitional year due to the current economic climate. Although we did not suffer such severe budget cuts imposed by the Ministry of Science and Innovation (MICINN) as other research institutions, our strategic plan was thwarted by both the budget cuts introduced in May as well as the grim predictions for 2011 announced prior to the summer. Indeed, the expected MICINN budget for 2011 will be 7.5% lower than that in 2010. This represents a steady decrease of 18% in non-competitive public funds (measured in constant 2004 EUR) over the past seven years. Although CNIO scientists continue to aggressively compete for external funding both in Spain and in the European Union, it is evident that we cannot maintain our previous growth rate under the current economic conditions.

It is during these difficult times that the support from our philanthropic partners is most appreciated. The continuous help from the *Fundación Caja Madrid* (Clinical Research Programme), *Fundación BBVA* (Cancer Cell Biology Programme), *Fundación Banco de Santander* (Genetic and Molecular Epidemiology Group), *Fundación "la Caixa"* (International PhD Programme), *Fundación Caja Navarra* (International Postdoctoral Programme), Avon (Breast Cancer Clinical Research Unit), *Catalana Occidente* (Visiting Scientists Programme) and *Iberia* (Travel support) maintains some of our key scientific activities. The support from an increasing number of collaborators (see pgs. 246-247) also provides additional resources for many activities that otherwise would not be possible with public funds. During 2010, we also attempted to attract substantial private funding to support our drug discovery efforts within the Experimental Therapeutics Programme (see below). Unfortunately, the Board of Trustees did not approve the financial proposal devised by the General Manager due to technical considerations. We can only hope that during 2011, the Board of Trustees will be able to resolve these issues and allow the CNIO to receive additional private funding.

In spite of current limitations, we were able to recruit two excellent young investigators to lead new research areas. Santiago Ramón-Maiques joined the Structural Biology and Biocomputing Programme as head of the Structural Bases of Genome Integrity Junior Group. Santiago trained with Wei Yang and Alasdair Steven at NIH, USA. His work

focused on the structural characterisation of the V(D)J recombinase. He also determined the crystal structure of the regulatory PHD finger of RAG2 in complex with histone H3, and the structure of the human DNA polymerase η , an enzyme whose deficiency causes a variant form of *X. pigmentosum*. Miguel Quintela-Fandino joined the Clinical Research Programme as Head of the Breast Cancer Junior Clinical Research Unit. Miguel trained with Tak Mak at the Ontario Cancer Institute, Canada, for four years. His work focused on the mechanism of invasion and metastasis in breast cancer. He complemented his training at the Princess Margaret Hospital in Canada, working for over two years on the development of several first-in-class anti-cancer drugs under the supervision of Lillian Siu. Miguel has received several honours including the ASCO Young Investigator Award and the ASCO Merit Award. He is the first of a group of young medical oncologists trained abroad that within the next three to five years should provide the CNIO with the necessary expertise to carry out competitive clinical research focusing on early phase clinical trials. Unfortunately, completion of the construction work at the *Hospital Universitario de Fuenlabrada* – where our clinical activities will be housed – was delayed due to the financial crisis. Work finally began in the Fall and will be completed in May 2011. This will allow us to more aggressively recruit young medical oncologists to staff our Clinical Research Programme.

Unfortunately two Group Leaders left the CNIO during 2010, Ángel Nebreda and Eduardo Moreno. Ángel decided to move to Barcelona for family reasons. Ángel and his research group left the CNIO in June 2010 to join the Institute for Research in Biomedicine (IRB). Ángel has been an extremely valuable asset to the Molecular Oncology Programme and we are thankful to him for his important contributions. Eduardo received a highly attractive offer from the University of Bern (Switzerland) and moved at the end of 2010. He has significantly contributed to the international visibility of the Molecular Oncology Programme with tremendous scientific output in the field of developmental biology. We were also saddened by the departure of Ralf Dahm, Director of Scientific Management, who has taken up a position at the newly founded Institute of Molecular Biology (IMB) in Mainz, Germany. Ralf has done a remarkable job during the time he has been with us and we wish him the very best in his new position.

As I indicated in the Foreword to the 2009 Scientific Report, I have expressed my desire to step down as CNIO Director providing that we can identify an internationally renowned scientist that will bring additional scientific expertise and new managerial know-how to the CNIO. In view of the lack of progress made during 2010, the Board of Trustees decided to recruit the services of a reputable head hunter company to identify 10 suitable candidates by year end. At the time of writing this Foreword, the Board of Trustees is considering two excellent candidates currently working in the USA and the UK. I hope that the Board will be able to offer an attractive package so a new Director can be recruited. In the meantime, as I informed the Board of Trustees in December, I will continue to serve as Director with the same dedication I have demonstrated over the last 12 years.

The decision to start up a drug discovery programme within the CNIO in 2006 is beginning to pay off. The concept behind the establishment of the Experimental Therapeutics Programme was to create an operational structure similar to that of a biotech company but integrated within the CNIO, sharing all its facilities and having close and continued interaction with CNIO basic and translational scientists. We reasoned that this would not only facilitate better use of available resources and scientific infrastructures, but also provide a research culture that is not always easy to implement in stand alone, small biotech companies. The research efforts carried out at the ETP are starting to show even earlier than anticipated. In October 2010 the first large patent covering various series of inhibitors for PI3Kinase, an enzyme mutated in one third of breast and colon adenocarcinomas, was published and granted to the CNIO. Additional patents covering different inhibitory profiles including a large array of compounds to protect the chemical scaffolds developed at the ETP have also been submitted. The next challenge will be to improve the preclinical portfolio of these compounds to make them attractive to major pharma companies so they can be developed and ultimately tested in clinical trials. To this end we have recently recruited the services of a small company specialised in establishing licensing agreements between academic institutions and small biotech companies with large pharma. We hope that some of these negotiations will pan out during 2011 so that our model for the ETP may eventually become a paradigm of how academic institutions can directly contribute to drug discovery efforts to benefit cancer patients.

Finally, I am very proud to report that the publication record of the CNIO Faculty continues to improve. According to a recent publication by the SCImago Institutions Ranking (SIR, www.scimagoir.com), the CNIO now ranks as the 13th best research institute in the world with a "Quality Output" of 88.18 (as a reference, the Whitehead Institute at MIT tops the list with a Quality Output of 93.75). This represents a significant improvement from last year when we ranked 21st. Since it is arguable that the criteria used by the SIR can be applicable to institutions (more than

2,800 World Wide) ranging from small research centres to large universities, we have decided to use our own benchmarking criteria. In short, we have compared the number of high impact publications in the 62 journals with an impact factor >15 published during a three year period (2007-2009), normalised by the number of principal investigators (PIs) working at the institution. To avoid giving equal value to our own publications versus collaborations, each publication was only counted once and ascribed to the institution housing the corresponding author.

When we carried out this benchmarking analysis with those institutions appearing at the top of the SIR list, the CNIO ranked second in the World (45 publications and 29 PIs yielding a ratio of 1.55 publications/PI) only behind the Whitehead Institute that has a staggering 3.74 publications/PI (71 publications and 19 PIs). Other prestigious research institutions including those appearing ahead of the CNIO in the SIR ranking had slightly lower ratios. The Rockefeller University with 148 publications and 111 PIs (a 1.33 ratio) and the EMBL with 60 publications and 47 PIs (a 1.28 ratio) immediately followed the CNIO. Six additional institutions including Fred Hutchinson Cancer Research Centre, Salk Institute, Sanger Centre, Vienna's Institute of Molecular Pathology, Dana-Farber Cancer Institute, Memorial Sloan-Kettering Cancer Center and Cold Spring Harbor also had ratios over 1 publication of IF>15 per PI. Since these data were obtained from the websites of these institutions, it is possible that small errors may affect these results. Moreover, the small differences observed among these premier research institutions should not be used to establish any type of formal "rankings". They do however represent an unbiased way to demonstrate that, based on its publication record, the CNIO is among the top research institutions in the World in the field of Life Sciences.

We have also compared the scientific output of the CNIO with that of other Spanish research institutions. During the 2007-2010 period, all research institutions in Spain generated a total of 640 publications (collaborations not considered) in journals with an impact factor >15. These publications corresponded to all fields of knowledge, not just the Life Sciences. Since the CNIO generated 55 of these publications, we can proudly state that the 29 PIs that worked at the CNIO during this 4 year period contributed almost 9% of the total national output in this selected category of publications. As a comparison, the whole Spanish University System with more than 80 universities generated 153 publications, less than 3 times as many as the CNIO.

I hope that these figures demonstrate to the scientific community, both at home and abroad, the quality of the research carried out at the CNIO. While it is difficult to translate this high quality research into immediate contributions that benefit cancer patients, we hope that the expansion of our drug discovery and clinical programmes will eventually enable this ultimate goal.