

The Spanish National Cardiovascular Research Center: A New Phase

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During the past century, it has become increasingly clear that scientific research is a source of wealth. Increasingly larger investments are made in R&D in the more highly developed countries, which have, in turn, helped to consolidate the privileged position of these countries. Research into healthcare is no exception, and investments in this area are considered not only a priority, but also an economic driver.

Clinical Research in Spain

During the seventies, Spanish biochemist Alberto Sols said that “conditions in Spain were not conducive to scientific research, but microclimates were starting to appear in which good research could be conducted.”¹ During the last 4 decades, biomedical research has improved significantly in our country. The evolution of scientific production in general and of biomedical research in particular, has been observed in several bibliometric studies.²⁻⁴ In an analysis of the 1996-2004 period made by Camí et al,⁴ it was seen that in comparison with the 1994-2002 period, eg, with a 2-year difference, scientific production in biomedicine had grown at the same rate as the entire scientific production of the country: 8.9% in the number of documents, 22.5% in the number of references appearing in other publications, and 12.5% in the number of references made per document. In the context of scientific production as a whole, biomedical research is ranked number 2 in terms of number of

documents, and is number 1 in terms of references appearing in other publications. An important finding of this study was the increase of almost 10% in international collaboration. Finally, when analysed by pathologies, production in the cardiovascular area occupies third place in terms of number of documents, after neurosciences and oncology.⁴

In spite of this unarguable growth, when we compare this with scientific production in other countries, things do not look so good, in such a way that during the abovementioned period studied, Spanish biomedical production accounted for 2.4% of the number of documents published on this research subject around the world, and 1.8% of references made in other works, which is far below what might be expected if we consider the socio-economic figures for our country.³

Likewise, a recent report published on research in the European Union (EU) focused on this issue, also hinting at the fact that the quantity and quality of scientific production in Spain are not parallel. Consequently, while Spain is ranked fifth among the 15 original countries making up the EU in terms of number of articles, it drops to seventh place in the number of references made in other works.⁵ Correlating these parameters with financing, the authors point out that in the 1994-2004 period, 1357 articles were published in our country per every 1000 million dollars invested in R&D, which puts us in third place after Germany and the United Kingdom; however, the number of references for the same amount invested was 1039, thus this parameter occupying 12th position.⁶

With regard to the percentage of GDP spent on R&D, the figures are not encouraging: Spain is in twelfth place among the 15 original EU member states (0.9%, as against the 1.9% average for the 15 states). It is important to point out that Ireland, a country that traditionally falls below the European average, spends 2.6% of its GDP, which has led to a considerable increase in scientific production. In addition, the Barcelona Declaration suggested that annual investment in R&D for the year 2010 should be around 3% of GDP, a goal that is still far from becoming a reality.

Finally, the biomedical research situation in Spain looks even more critical when we compare it to that found

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in Europe and the United States. The latter country spends 2.7% of GDP on R&D (2003 figures). In addition, the productivity of the 15 EU member states is equal to 75% of the productivity in the United States.⁶

The growth of scientific production in biomedicine in our country during recent decades can be attributed to multiple factors; among these, it is important to note the active scientific policy adopted by successive governments and the autonomous communities, the training and incorporation of an increasing number of scientists and the fostering of their international contacts, the appearance of new sources of financing, both domestic and from the EU, and the involvement of hospital healthcare personnel in clinical research. The importance of this final factor can be seen from the fact that 47% of biomedical articles are signed by healthcare professionals at a healthcare centre.³

One of the problems with clinical research during recent decades has been the fragmentation of groups and their relative distance from basic research.^{7,8} For more than a decade, the management of the National Institutes of Health (NIH) in the United States has recognised the need to facilitate cooperation between basic and clinical researchers by improving their training and making particular efforts to finance clinical and translational research. Other countries have followed this line of action, and have created their own programmes for developing and promoting clinical and translational research.⁹

This problem can also be seen in Spain, where it also has very specific causes. The low level of relevance given by hospital managements to the research activities of their doctors, without having promoted or even recognised the need to devote a percentage of the working day to this activity, and the zero repercussion of scientific merit on their professional careers have hindered the formation of powerful cores of clinical researchers. In addition, this activity offers few attractions to young people in training in comparison to haemodynamics and electrophysiology.

In a very recent bibliometric study sponsored by the CNIC and performed by the BAC group in Barcelona (Agència d'Avaluació de Tecnologia i Recerca Mèdiques [AATRM], Parc de Recerca Biomèdica de Barcelona [PRBB], and Universitat Pompeu Fabra [UPF]), Spanish scientific production in the cardiovascular area was analysed (including research into vascular cerebral pathologies) during the 1996-2004 period from a different standpoint.¹⁰ The purpose of the study was to identify groups of clinical researchers in this field and to analyse their scientific production. In order to do this, an algorithm was used that detected collaboration between authors, the stability of this cooperation and the preferred specialisation in the area studied. A total of 79 groups with 691 authors in Spanish centres and 301 located in foreign institutions were identified. The 79 groups published 3144 documents during the period, representing only 44% of all the documents published by Spanish centres on this subject. The study also pointed out the

great variations among the autonomous communities, with a higher level of group concentration in Madrid and Catalonia and hardly anything in the other regions.

Thematic Networks and CIBER

The abovementioned deficiencies in the structure of clinical research led the Ministry of Health and its body in charge of biomedical research, the Instituto de Salud Carlos III (ISCIII), to create thematic networks and subsequently, the Network Biomedical Research Centres (Centros de Investigación Biomédica en Red - CIBER), in an attempt to promote cooperation among researchers. As the ISCIII web page defines it: "The thematic networks for cooperative research (RTIC – Redes Temáticas de Investigación Cooperativa) are organisational structures formed by the association to the Instituto de Salud Carlos III of a variable set of biomedical centres and research groups, of a multidisciplinary nature, dependent on the different Public Administrations or the private sector and owned by a minimum of 4 autonomous communities, the purpose of which is to conduct cooperative research projects of general interest."

CIBER is one more step towards integrating researchers, and is defined as: "a research body having legal personality, whose mission is the monographic research into a specific pathology or health problem, defined in wide terms. It is made up by research groups, without physical contiguity, belonging to different Administrations, Institutions, or Autonomous Communities, of the public or private sector..."¹¹ CIBER have been created in different areas, but not in cardiology or oncology, coinciding with the existence of the 2 corresponding national centres, CNIC and the National Centre for Oncological Research (Centro Nacional de Investigaciones Oncológicas - CNIO).

The importance of this new networking model in cardiovascular research has been highlighted by 3 special articles published in this edition of the *Revista Española de Cardiología*, and its actual dimension is being translated, undoubtedly, into more scientific production, more cooperation among basic and clinical researchers and more Spanish clinical research published in journals with an impact on our speciality. In this network organisation, what is the CNIC and what can it offer?

What Is the CNIC?

The Carlos III National Centre of Cardiovascular Research Foundation is an institution sponsored by the ISCIII, the purpose of which is to encourage research into cardiovascular diseases by creating and maintaining the CNIC.

With the creation of this centre, the aim was to provide the country with an excellent cardiology research infrastructure, the purpose of which can be summarised in the following points:

- To conduct excellent basic research in the cardiovascular area
- To participate in the training of new researchers in the cardiovascular area
- To promote the translation of knowledge from basic research to patients' care
- To collaborate with the National Health Service and with scientific societies to promote cardiovascular research and health in Spain
- To collaborate, advising healthcare authorities on the aspects of cardiovascular diseases that they consider appropriate

It is clear from these objectives and the mood of the researchers and the scientific management of the CNIC that the institution must be at the service of patients and professionals of the National Health System, without competing or duplicating structures that already exist within Spanish cardiovascular research.

The CNIC has been organised into 6 departments (Table 1), 3 of them basic and 3 of them with an outside projection. The departments integrate into a research committee presided over by the scientific vice-president, and the whole structure is managed by the Scientific President (V. Fuster). In addition, the CNIC has technical units, the number of which is being increased to meet the researchers' growing needs.

The CNIC headquarters is a 23 000 m² building, laid out over 7 floors and situated on the ISCH Campus. It has capacity for 300 researchers and currently houses 200 of them and a further 100 support staff, including administrative staff, scientific management, librarians, and computer specialists, among others. The translational research department has its headquarters in Barcelona thanks to an agreement between CNIC and the Hospital Clínic.

What Can the CNIC Contribute to Cardiovascular Research?

The need for and the efficiency of monographic research centres as opposed to network researching or CIBER has been questioned in some areas. The main criticism lies in the possibility that a centre of this nature could become isolated, without connection with clinical activity. In its current stage, which started approximately 2 years ago, the scientific management of CNIC is fully aware of this risk and is working to prevent isolation, to integrate the Spanish research centre and relate it to the National Health System (NHS).

The CNIC also contributes some peculiarities that can serve as a model in the future for other similar institutions. In the first place, one of the most innovative aspects is its financing system. On 15 December 2005, the President of the Spanish Government presided over the signature of an agreement by way of which some of the most important Spanish companies made a commitment to the

TABLE 1. Scientific Equipment of CNIC

Departments	Units
Vascular biology and inflammation	Proteomics
Developmental biology	Genomics
Regenerative cardiology	Animal house
Atherothrombosis and cardiovascular imaging	Microscopy
Epidemiology and Population Genetics	Cytometry
Translational Cardiovascular Research	Transgenesis

Ministry of Health and Consumer Affairs to finance a significant part of the maintenance and research activities of the CNIC, through the creation of the Pro-CNIC Foundation. The constitution of this foundation to channel aid from business to the CNIC is the most important company sponsorship activity of recent years in terms of its sum, social relevance, the group of companies it comprises and the results foreseen. The project also establishes the mechanisms by which the companies participating can intervene in relevant decisions and in the design of the CNIC activities, through their participation in the board of trustees, and providing stable financing for the project.

Secondly, this financing has enabled a critical mass of experimental researchers to be concentrated in a modern centre with full technology equipment. The interaction between basic groups of different origins and training, in a competitive environment where it is possible to develop an entire professional career, this is permitting an appropriate scientific environment to be created for a centre of this nature.

A third important element is the outward projection of the CNIC. In spite of the fact that it has no patients and no facilities for clinical research, the institute has 3 departments: Image, Epidemiology, and Translational, whose main activity will be developed in collaboration with hospitals and NHS care centres through specific agreements with certain centres, coordinating studies, promoting and financing clinical research or supporting this from the CNIC laboratories and units.

Several actions are being conducted with this objective. First of all, the researchers from the different departments and technical units of the CNIC form part of the RETIC represented in this edition of the *Revista Española de Cardiología*. Secondly, the CNIC has launched a call coordinated by the Translational Research Department, which will finance research projects facilitating the conversion of knowledge generated by basic research into improvements in clinical practice. In order to achieve this, it will distribute up to three million euros every year, with the possibility of financing up to one million euros per project. The call of proposals, which is currently in the project evaluation and selection stage, has received 15 projects from these together with researchers from 40 institutions: 15 hospitals, 13 institutes or research centres,

8 universities, 1 private clinic, and 3 foreign institutions. In addition, a laboratory from the CNIC itself is participating in 5 of the 15 projects. With the aim of ensuring maximum objectivity and independence, the evaluation is carried out by foreign researchers of recognised prestige and coordinated by the FIS Cardiovascular Research Commission. With this measure, the CNIC hopes to establish lines of communication and collaboration among the basic researchers themselves and the most relevant clinical researchers in the country.

Finally, the Translational and Epidemiological departments have the purpose of developing the infrastructure necessary to give support to the clinical research in other centres, including areas such as IT, biostatistics, clinical trial design, and information on regulatory aspects.

Training is one of the basic objectives of the CNIC, for the purposes of which the centre has developed a general training plan, called CNIC-Joven, which covers all levels, from basic secondary education to post-doctorate training. The training plan is structured into the following initiatives:

- Pre-doctorate CNIC programme: aimed at young graduates in a biomedical science for doing a doctoral thesis

- Post-doctorate programme: aimed at PhD in biomedical science. The basic aim of this programme is to attract young researchers (both from Spain and abroad) to provide them with excellent training in some cardiovascular research areas developed in the laboratories at our centre. Some of the research projects will also be conducted in collaboration with international centres with which the CNIC has entered into collaborative training agreements

- Acércate (“Approach!”) programme: aimed at final-year secondary education students, giving students the opportunity to spend a few weeks learning new techniques applicable to biomedical research, doing directed experiments and learning how to use some sophisticated scientific equipment under the supervision of the researchers at the centre

- Cicerone programme: aimed at second-cycle university students studying subjects related to biomedicine. It offers the possibility of making contact with biomedical research and completing their training through work placements in laboratories during the summer months

- Cicerone Day: aimed at medical professionals during their internship period, second-cycle university students studying biomedical science and pre-doctorate researchers. The purpose of this workshop is to serve as a general guide into the field of cardiovascular research in our country, as well as offering attendees the opportunity to come into direct contact with the “leaders” in this field

- INVESMIR programme: aimed at medical professionals during their residency period. It permits a

stay, during the optional rotation period, in a CNIC laboratory participating in a research project

In the specific field of clinical research, an ambitious training programme has been developed for clinical researchers who may join the NHS in the future:

- Cardiojoven (“Young Cardio”) programme: aimed at doctors who have finished their internship in a speciality related in some way to the cardiovascular area. The programme has been designed to provide theoretical training and includes basic, clinical, and epidemiological aspects. The participants will develop part of their research projects at the CNIC, part in other centres belonging to NHS and even in international research centres such as the Mount Sinai Medical Centre or Johns Hopkins University, by virtue of agreements with these institutions

Finally, the CNIC, in collaboration with the Spanish Cardiology Society, participates in the continuous training of cardiologists via courses, such as that on Cardiovascular Pathophysiology. Its purpose is to offer a translational view of cardiology, bringing doctors into contact with the study of pathophysiology and basic research, showing them the molecular and genetic basis of heart diseases and giving them, at the same time a modern view of cardiac physiology.

In short, the CNIC constitutes a new experience in the field of cardiovascular research in Spain. The aim is to achieve excellent basic research and to encourage its translation to clinical practice through cooperation with networks and NHS centres and hospitals. In this context, the discovery and training of new researchers constitutes an essential element in this new stage.

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