Cooperative Cardiovascular Disease Research Network (RECAVA)

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Today, cardiovascular disease is the principal cause of death and hospitalization in Spain, and accounts for an annual healthcare budget of more than 4000 million euros. Consequently, early diagnosis, effective prevention, and the optimum treatment of cardiovascular disease present a significant social and healthcare challenge for the country. In this context, combining all available resources to increase the efficacy and healthcare benefits of scientific research is a priority. This rationale prompted the establishment of the Spanish Cooperative Cardiovascular Disease Research Network, or RECAVA (Red Temática de Investigación Cooperativa en Enfermedades Cardiovasculares), 5 years ago. Since its foundation, RECAVA's activities have focused on achieving four objectives: a) to facilitate contacts between basic, clinical, and epidemiological researchers; b) to promote the shared use of advanced technological facilities; c) to apply research results to clinical practice; and d) to train a new generation of translational cardiovascular researchers in Spain. At present, RECAVA consists of 41 research groups and 7 shared technological facilities. RECAVA's research strategy is based on a scientific design matrix centered on the most important cardiovascular processes. The level of RECAVA's research activity is reflected in the fact that 28 co-authored articles were published in international journals during the first 6 months of 2007, with each involving contributions from at least 2 groups in the network. Finally, RECAVA also participates in the work of the Spanish National Center for Cardiovascular Research, or CNIC (Centro Nacional de Investigación Cardiovascular), and some established Biomedical Research Network Centers, or CIBER (Centros de Investigación Biomédica en RED), with the aim of consolidating the development of a dynamic multidisciplinary research framework that is capable of meeting the growing challenge that cardiovascular disease will present in the future.

Key words: Traslational medicine. Investigational networks. Formation.

Red Temática de Investigación Cooperativa en Enfermedades Cardiovasculares (RECAVA)

Actualmente, las enfermedades cardiovasculares constituyen la primera causa de muerte y de hospitalización en España, y además generan un gasto sanitario anual superior a los 4.000 millones de euros. El diagnóstico precoz, la prevención efectiva y el tratamiento óptimo de las enfermedades cardiovasculares constituyen pues un auténtico desafío sociosanitario para nuestro país. En este contexto, resultaba prioritario unificar los recursos disponibles para potenciar la eficacia científica y la rentabilidad asistencial de la investigación cardiovascular, lo que originó la creación, hace 5 años, de la Red Temática de Investigación Cooperativa en Enfermedades Cardiovasculares (RECAVA). Durante este tiempo, el quehacer de RECAVA se ha centrado en la consecución de un cuádruple objetivo: a) facilitar la interrelación de los investigadores básicos clínicos y epidemiológicos; b) fomentar el uso compartido de recursos tecnológicos complejos; c) transferir a la asistencia clínica los resultados de la investigación, y d) formar la nueva generación de investigadores traslacionales cardiovasculares españoles. En el momento actual RECAVA está constituida por 41 grupos de investigadores y 7 plataformas tecnológicas de uso común. El plan estratégico de investigación de RECAVA está organizado a partir de un diseño científico matricial basado en los procesos cardiovasculares más relevantes. Una muestra de la actividad investigadora de RECA-VA se plasma en el hecho de que en los primeros 6 meses de 2007 se han publicado 28 artículos cooperativos en revistas internacionales, con participación de al menos 2 grupos de la red. Finalmente, RECAVA coopera con el Centro Nacional de Investigación Cardiovascular (CNIC) y con algunos de los Centros de Investigación Biomédica en RED (CIBER) existentes, al objeto de consolidar una estructura de investigación multidisciplinaria y dinámica capaz de afrontar los retos de magnitud creciente que comportarán las enfermedades cardiovasculares en el futuro.

Palabras clave: *Medicina traslacional. Redes de investigación. Formación.*

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INTRODUCTION

The Challenge of Biomedical Knowledge Transfer in the Field of Cardiovascular Diseases

It is well know that transfer of biomedical knowledge to the health system gives rise to important social and economic benefits. However, we must be aware of the ever widening chasm between the fast and abundant generation of biomedical knowledge and its limited and slow application in practice. The lack of funds for applied biomedical research is an important cause of this phenomenon, but not the only one. Another important barrier is the complexity of the administrative guidelines and requirements, which usually overwhelm those involved in independent academic research. In addition, the knowledge generated by investigation is patchy and does not deal head-on with clinical problems, giving rise to isolated pools of sometimes contradictory and often irrelevant or only partially relevant data. Mechanisms are required to integrate these partial and dispersed observations into useful knowledge, that is, an integrated body of knowledge with predictive value. Likewise, there are no mechanisms to facilitate the exchange of knowledge among clinical and nonclinical investigators. For example, the preclinical research that research that can, in theory, be applied—is often performed in settings far removed from health care and clinical processes. The distance between academic research and private companies is greater still: at the same time that biomedical researchers come up against almost insurmountable problems to convert their discoveries into practicable strategies, the industrial sector stands impassively by while the success rate for bringing products to the market decreases at the same rate that the complexity, costs of production processes, and requirements for profitability in a globalized and increasingly competitive economy increase. By and large, this disjointedness is the result of the true Achilles heel in translating biomedical knowledge: the lack of clinician scientists and basic scientists with clinical vision, that is, clinicians with a solid scientific training and biologists, biochemists, physicists, and mathematicians with a clinical/health care perspective who act as intermediaries in the 2-way flow of knowledge.

The need to overcome these barriers is particularly relevant in the area of cardiovascular diseases due to the huge health care and socioeconomic repercussions of these problems. In effect, innovations in this area have been the drivers behind the increase in life expectancy in Western countries, which in turn has also had a huge effect in terms of economic growth. Although these achievements are legitimate grounds for pride and optimism, they have also given rise the widespread belief that cardiovascular diseases are relatively easy to prevent and overcome. It is also held that these diseases only affect the elderly and are relatively uncommon in Mediterranean countries. This could not be further from the truth. Cardiovascular diseases are the leading cause of death in developed countries and before 2020 they will become the leading cause of death worldwide. In Spain, this group of diseases is the leading cause of death and hospitalization and the third most important cause of reduction in disability-free life expectancy after mental illness and cancer. Furthermore, they generate an annual cost of more than €4000 million, equivalent to 7.1% of the health budget of the Spanish social security, with a total estimated cost of €6997 million a year.¹

One of the underlying causes for the growth in cardiovascular diseases is, along with the unfavorable changes in lifestyle and the aging of societies in the developed world, the ignorance of the mechanisms associated with their development. For this reason, the advances in recent decades concerning prevention and treatment have only served to delay the appearance of these diseases or to palliate their effects, but not to prevent or cure them. Unfortunately, the recent explosion in new sciences (genomics, proteomics, information, etc) has yet to lead to tangible benefits for cardiovascular patients.

RECAVA Response: History and Achievements

The RECAVA network was founded in 2002 as a result of the call for proposals for Redes Temáticas de Investigación Cooperativa (Thematic Networks for Collaborative Research—RETICs) made by the Instituto de Salud Carlos III (Decree SCO/709/2002 dated March, 22) to respond to the challenge outlined above and to contribute to reducing the impact of cardiovascular diseases on survival and quality of life of Spanish citizens. The guiding principle in the creation of the network was the conviction that coordination of the different basic research, clinical, and epidemiological groups in Spain in the cardiovascular field should give rise to consolidation of an efficient network able to: a) facilitate synergies among these groups and progressively incorporate others, thereby promoting a coordinated effort; b) take advantage of the Spanish national health system, as yet underused, for transferring and promoting cardiovascular research in hospitals; and c) obtain results that might actually contribute to improving public cardiovascular health and reinforce the competitive advantage of Spanish biomedical research in the European and international framework.

In the 3 years since the first call for proposals, the network grew in accordance with these initial goals, as reflected by the following achievements: *a*) real collaborative operation by bringing and binding together a very diverse set of centers and disciplines with little or no previous experience in networked research;

b) accumulation and availability to researchers of a vast body of information and study material, of a very varied nature, including, of particular note, clinical, and epidemiological databases (more than 8000 individuals included in multicenter collaborative studies) and collections of biological samples (9650 samples); c) a large number of publications with increasing scientific impact (208 publications that specifically cite the network); d) real transfer to clinical practice of preclinical or epidemiological knowledge, with studies in areas such as myocardial regeneration with different cell types, protection of the myocardium against severe ischemia, or research into health care models through large registries of cardiovascular clinical practice (MASCARA study); e) setting up and consolidation of 7 technology platforms; f) initiation and development of different coordinated projects that have successfully applied for a range of grants and that involve many centers of the network in different combinations; and g) training activities, with a large number of exchange programs to enable researchers to work in the different nodes of the network (more than 150), to which we should add several courses and scientific meetings under the umbrella of RECAVA.

The latest call for proposals for RETICs (Official State Journal, No. 145, dated June 19, 2006) made by the Instituto de Salud Carlos III has allowed of RECAVA to be recast in accordance with the spirit and possibilities of the call, the previous experience described above, the capital accumulated in the previous stage, the expected progress of other centralized or networked Spanish research projects in the cardiovascular field, and the imperious need to overcome the barriers that block the transfer of biomedical knowledge, taking advantage of the real competitive advantages offered at present by Spanish cardiovascular research.

RATIONALE

The importance of cardiovascular diseases raises several challenges to society as a whole, and the medical community in particular²: the cultural challenge of modifying lifestyles to make them healthier from childhood; the health care challenge of optimizing preventative and health care resources to reduce the impact of these diseases on the health of the population; the academic challenge of implementing multidisciplinary training in cardiovascular medicine to make possible an integrated care for patients who, by definition, have systemic diseases; and finally the scientific challenge of developing a research model that enables the application of current scientific resources in the generation of innovative knowledge with real application in health care.

The research model that can best respond to the scientific challenge described above is that of translational research, that is, the search on the one hand for solutions to real health care and clinical problems in the knowledge generated by laboratory experiments and, on the other, the search for diagnostic and therapeutic applicability of this knowledge through clinical trials and health campaigns. This is, therefore, a 2-way process: from the population and patient to the molecular level and from this level to the patient and the community. This was conceptual framework in which RECAVA was born and has prospered. In recent years, a research model has appeared which is facilitating networking-with sharing of knowledge and interests among basic, clinical, and epidemiological scientists dedicated to cardiovascular disease in Spain-as well as the creation of a platform of action that avoids duplicating effort and facilitating the pooling of resources. Within RECAVA, special emphasis has been placed on the training of young basic and clinical scientists able to implement the translational model of cardiovascular research in Spain.

OBJECTIVES, PROJECTS, AND ORGANIZATIONAL STRUCTURE

With the above as the foundation, the strategic plan of RECAVA revolves around the axes described in the following sections.

Development of a Scientific Grid Structure Based on the Most Relevant Cardiovascular Processes

Clinical disease defines the conceptual axis of the network. To carry out its mission, the network should be organized in cross-sectional programs—identified as priority lines of investigation—which should be applied, in a multidisciplinary and complementary fashion, to the study of cardiovascular processes (longitudinal lines) with greater social and health repercussion and greater impact on life expectancy and quality of life (Figure 1, lines of investigation). Within this general framework, several priority research programs have been identified (Table 1), and the initial results have already been published.⁶⁻²²

Organizational Structure of the Network

The current structure of RECAVA is the result of 2 major actions: the selection of a set of groups of excellence and the implementation of a solid and representative system of governance. After an anonymous external preselection process and after evaluation and subsequent selection by the Instituto de Salud Carlos III, the new RECAVA is made up of a total of 41 groups which, in accordance with the terminology established by the Instituto de Salud Carlos III (Official State Journal No. 145, dated June 19, 2006), are classed as research groups (22) and clinical/health care groups

TABLE 1. Priority Research Programs

Characterization of new mechanisms of myocardial growth and dysfunction with implications for diagnosis using markers and therapeutic targets in different heart diseases that involve left ventricular hypertrophy and that progress to heart failure

Identification of mutations associated with the development of hereditary heart diseases, analysis of the correlation between genotype and phenotype, and study of the pathophysiological mechanisms implicated in the clinical expression of the different mutations

Relationship between insulin resistance and cardiovascular disease Chronic ischemic heart disease and acute coronary syndromes Ischemia-reperfusion injury

Cell therapy

Pathogenic and epidemiological characterization of aortic valve stenosis

Characterization of dysfunctioning myocardium

(19) (Table 2). To these, 7 technology platforms of common usage should be added (Figure 1, platforms). The governance structure (Figure 1) aims to be as representative as possible of the interests of the different groups and contains the following elements: a) a governing body, the Administrative Board, in which all groups of the network are represented; b) an executive body, the Executive Committee, which—through the General Coordinator and the Research Manager-is responsible for control of the general coordination and operation of the network, with logistic support from the Technical Secretary of the network; and c) an External Scientific Committee for the network, which is considered essential for its consultancy role and to ensure an external control of the operation of the network.



Figure. 1. Organizational structure, platforms, programs, and lines of research of RECAVA. The research groups are the most important and are fully represented on the Administrative Board, the governing body that oversees the network operation by means of the Executive Committee. CIMA indicates Center for Applied Medical Research; CVD, cardiovascular diseases; HULP, Hospital Universitario La Paz; HUVH, Hospital Universitari Vall d'Hebron de Barcelona; IACS, Aragon Institute for Health Sciences; ICICOR, Valladolid Institute for Heart Sciences; UAM, Universidad Autónoma de Madrid.

TABLE 2. Groups That Currently Make Up RECAVA

Research Groups	Health Care/Clinical Groups
 Andrés García, Vicente (Instituto de Biomedicina, Valencia) Boscá Gomar, Lisardo (IIB, CSIC, Madrid) Cachofeiro Ramos, Victoria (Universidad Complutense, Madrid) Castro-Beiras, Alfonso (Complejo Hospitalario Juan Canalejo, A Coruña) Civeira Murillo, Fernando (Instituto Aragonés de Ciencias de la Salud, Zaragoza) de la Pompa Minués, José Luis (CSIC-CNB, Madrid) Diez Martínez, Javier (CIMA, Pamplona) Egido de los Ríos, Jesús (Fundación Jiménez Díaz, Madrid) España Furió, Francisco (Hospital Universitario La Fe, Valencia) Fernández-Avilés, Francisco (Hospital General Universitario Gregorio Marañón, Madrid) Fontcuberta y Boj, Jordi (Hospital de la Santa Creu i de Sant Pau, Barcelona) García-Dorado, Antonio David (Hospital Universitario Vall d'Hebron, Barcelona) Gabriel Sánchez, Rafael (Hospital La Paz, Madrid) Martínez González, José (CSIC-ICCC, Barcelona) Mayor Menéndez, Federico (Centro de Biología Molecular Severo Ochoa. Facultad de Ciencias. Universidad Autónoma, Madrid) Ordoñez Fernández, Antonio (Hospital Universitario Virgen del Rocío, Sevilla) 	 Alonso Martín, Joaquín (Hospital de Fuenlabrada, Madrid) Álvarez-Sala Walter, Luis (Hospital General Universitario Gregorio Marañón, Madrid) Ancillo García, Pablo (Hospital General de Segovia) Bethencourt González, Armando (Hospital Son Dureta, Palma de Mallorca) Blanco Varela, Jesús (Hospital del Río Hortega, Valladolid) Bosa Ojeda, Francisco (Hospital de Canarias, Santa Cruz de Tenerife) Casasnovas Lenguas, José Antonio (IACS, Zaragoza) Gallego Page, Juan Carlos (Complejo Hospitalario de Albacete) García Puig, Juan (Hospital La Paz, Madrid) Gimeno Blanes, Juan Ramón (Hospital Virgen de la Arrixaca, Murcia) Iñiguez Romo, Andrés (Complejo Hospitalario do Meixoeiro, Vigo, Pontevedra) López Bescós, Lorenzo (Hospital de Alcorcón, Madrid) López Sendón, José Luis (Hospital de la Paz, Madrid) López-Messa, Juan (Hospital Río Carrión, Palencia) Manito Lorite, Nicolás (Hospital de Bellvitge, L'Hospitalet de Llobregat, Barcelona) Muxí Pradas, María África (Hospital Clínic i Provincial, Barcelona) Martínez Ferrer, José (Hospital de Txagorritxu, Vitoria, Álava) Querejeta Iraola, Ramón (Hospital de Donostia, San Sebastián, Guipúzcoa) Tobaruela González, Agustín (Hospital Juan Ramón Jiménez, Huelva)

CIMA indicates Center for Applied Medical Research; CNIC-CIB, Spanish National Center for Cardiovascular Research-Biological Research Center; CSIC-CNB, Spanish National Research Council-National Center for Biotechnology; CSIC-ICC, Spanish National Research Council-Catalan Institute for Cardiovascular Research.

Training Plan

The overall goal of the training plan of RECAVA is to forge teams of clinical and basic researchers able to share a system of study of clinical/health care problems in the cardiovascular field with a view to effective transfer of the contributions of cardiovascular biological sciences to actual health care of cardiovascular patients.^{4,5} This program has the following specific objectives: a) to provide the clinical investigators with the necessary knowledge and skills to carry out investigation that probes the underlying biology of cardiovascular diseases (Table 3); b) to provide basic researchers with the necessary knowledge and skills to carry out research aimed at diagnostic and therapeutic progress in cardiovascular diseases (Table 3); c) to promote teamwork in clinical and basic research by developing collaborative projects; and d) to encourage basic and clinical scientists to transfer the findings of their collaborative research to the health system for evaluation and subsequent application.

Two instruments have been used for the development of the program: an academic course and an exchange

TABLE 3. Specific Goals of the RECAVA Training Plan

Goals for clinicians (and basic scientists) Handling of basic molecular technologies Taking and handling biological samples Bioinformatic analysis of the data obtained Handling of the population aspects of application of the results Goals for basic scientists (and clinicians) Identification of clinically useful genotype-phenotype associations Identification of diagnostic markers (biological-physical) Identification of therapeutic targets Identification of optimum therapies from the molecular standpoint

program. The academic course is conceived as a 3-day face-to-face course every year. Those who take the course are young clinical and basic researchers who come from any of the centers of the network. The lecturers are national and foreign investigators, with extensive experience in translational cardiovascular research, who develop a course structure of practical situations representative of the lines of research of the network, ranging from the general population to the molecular level, and including the individual patients, and from the molecular level back to the general population. The exchange program of investigators includes stays for network investigators in centers other than their own, in order to intervene directly in the research of a collaborative project in which their own center and the host center are participating. In addition, the program includes a second type of stay in centers in which the RECAVA platforms are located so that the investigators become familiar with how these work and how they apply to specific network projects in which their center may or may not be implicated.

Other Strategic Actions

Obviously the productivity of the scientific project, the organizational structure, and training are the main determinants of the future performance of the network, but for success, other strategic actions should be taken, in particular: a) development of specific programs that help obtain the best performance from the research actions of the groups, including the coordination program for health care groups, the quality control and internal assessment program, the program for European projects, and the program for institutional relations; b) enhancement of common platforms; c) planning for dissemination and transfer of the findings of the research to the scientific community, society, and the productive system; d) mobility planning, to improve research competitiveness of the members of the network through stays in centers belonging to the network or foreign centers; and e) system for assessing the network through application of periodic indicators of structure, processes, and results of scientific output of the network.

RESULTS

Network Operation and Collaborative Activity

One of the requisites for RECAVA to attain its goals is for a large number of collaborative activities to be carried out involving different centers in the network. The analysis of collaborative activity done in the 6 months since initiating the new RECAVA project shows a substantial and rapidly increasing volume of scientific collaborations within its structure. If we limit ourselves to ongoing collaborations, that is, those that have already provided tangible (although not necessarily definitive) results, the map of collaborative activity is that reflected in Figure 2. The network of connections shown in Figure 2, in which the participation of all the research groups and many of the clinical/health care groups can be discerned, also illustrates the central role of translational research in our network: most of the collaborative activities are organized around a core of centers that generate strong clinical and research activity.

The same analysis showed substantial activity in the exchange of samples. During the first 6 months of 2007, a total of 55 exchanges were made (corresponding to hundreds of samples) of both human material (31 exchanges) and animal material (24 exchanges), ranging from plasma and serum to DNA samples, or biopsies to cell lines and transgenic animals.

Publications

Although scientific output might not be expected during the first year of operation of a collaborative research network, this is not the case for RECAVA given that it is a reformed version of an already existing network. An analysis of publications, probably incomplete, shows that in addition to studies published during the initial stages of the network (2002-2005) and during the so-called "bridging project" period in 2006, during the first 6 months of 2007, at least 28 articles have been published in international journals with the participation of at least 2 RECAVA groups. A point worth highlighting concerning this collaborative output is that it is published in both essentially experimental journals (Cardiovascular Research or Journal of Mass Spectroscopy) and in essentially clinical journals (European Heart Journal, American Journal of Medicine), or journals that cover both fields (Journal of Hypertension, Blood).⁶⁻²²

Transfer of Results

The ultimate mission of RECAVA is to improve cardiovascular health in Spain and the general population, and so the translational results are considered particularly important. Thus, in the near future, RECAVA hopes to complete transfer to clinical practice of results obtained in the laboratory. Of note are areas such as cell transplantation (pending phase 2-3 multicenter clinical trials) and cardioprotection by extending acidosis during reperfusion or by pharmacological treatments (at the beginning of the clinical phase), both applicable in patients with acute myocardial infarction. Likewise, soon it is hoped to transfer the results of epidemiological studies to clinical practice. Of particular note is the MASCARA study (optimization of available therapeutic strategies in acute coronary syndrome, whose results have recently been analyzed).

Central Units

All units planned initially have become operative and more importantly—are being actively used by the groups of the network.

Coordinated Projects

The network has managed to ensure that most of the affiliated groups have initiated scientific research projects



Figure. 2. Collaborative research between RECAVA groups in June 2007. The groups are represented by their abbreviations (adjacent table), with research groups in black and health care/clinical groups in red. The connecting lines between 2 groups correspond to ongoing collaborative research activities (defined as those that have produced some findings). CBM indicates Severo Ochoa Madrid Center for Molecular Biology; CIMA, Center for Applied Medical Research, Pamplona; CNB, National Center for Biotechnology; CNIC, National Center for Cardiovascular Research: CRH. Regional Center for Blood Donation, Murcia; CSIC, Spanish National Research Council; FJD, Jiménez Díaz Foundation; FM, Federico Mayor; HB, Hospital de Bellvitge; HCV, Hospital Clínico Universitario de Valladolid; HDLP, Hospital de la Princesa de Madrid; HF, Hospital de Fuenlabrada; HGGM, Hospital General Universitario Gregorio Marañón; HGS, Hospital General de Segovia; HJC, Hospital Juan Canalejo de A Coruña; HLF, Hospital La Fe de Valencia; HLP, Hospital La Paz de Madrid; HMS, Hospital Miguel Servet de Zaragoza; HRC, Hospital Río Carrión de Palencia; HRH, Hospital del Río Hortega de Valladolid; HSP,

Hospital de la Santa Creu i de Sant Pau de Barcelona; HUVH, Hospital Universitario Vall d'Hebron de Barcelona; HVA, Hospital Virgen de la Arrixaca de Murcia; HVR, Hospital Virgen del Rocío de Sevilla; ICCC, Catalan Institute for Cardiovascular Science; INM, Immunology Department of the Universidad Autónoma de Madrid; IVB, Vascular Biology Laboratory of IBV; LGM, Lipid Unit of the Hospital General Universitario Gregorio Marañón; UAM, Universidad Autónoma de Madrid; UCM, Universidad Complutense de Madrid.

in collaboration, thereby attaining the main goal. Likewise, under the RECAVA umbrella, applications have been made for a total of 7 collaborative projects in the Spanish Health Research Fund call for proposals, 11 projects in the call for independent clinical research proposals, 5 in the CNIC call for proposals, and at least 2 in the 7th Framework Program.

Training Activities

In March 2008, the first International Symposium on Translational Research in Cardiovascular Diseases is to be held. This will form the basis for an academic course attended by young members in training who belong to the different centers of the network. On the other hand, during 2007, more than 10 researchers have participated in the network exchange program.

Infrastructures

The operation of the network has been helped by the implementation of different information and communication infrastructures, with the interactive Internet gateway (http://www.recava.com) being of particular note. This gateway allows not only the dissemination and exchange of information but also the pooling of computing resources (applications, databases) for coordinating and managing collaborative network research in a secure and efficient fashion.

CLOSING REFLECTIONS

In short, RECAVA has proved an efficient tool for promoting translational research in cardiovascular diseases in Spain. In fact, it has created synergies among groups and information exchange among basic scientists, clinicians, and epidemiologists. It has also promoted collaborative research with the aim of rapid transfer of the basic biomedical findings to clinical practice and health care of the population. It is foreseen that the results of this effort will become evident in the coming years, with the culmination of ongoing collaborative studies. On the other hand, RECAVA has a huge potential for training research personnel and facilitating exchange of information and techniques, as well as for generating the shared intellectual environment required by translational research in cardiovascular diseases. In this type of research, long-term work is important to obtain valid and useful achievements. It follows then that RECAVA, as a tool for implementing this type of research into cardiovascular diseases in Spain, is an investment in the future by our scientific bodies and health authorities. Finally, both the committee and all members of the network should consider RECAVA as a dynamic network open to the future integration of new research groups.

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REFERENCES

- Leal J, Luengo-Fernandez R, Gray A, Petersen S, Rayner M. Economic burden of cardiovascular diseases in the enlarged European Union. Eur Heart J. 2006;27:1610-9.
- Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. Plos Med. 2006;3:2011-30.
- Marincola FM. Translational medicine: A two-way road. J Transl Med. 2003;1:1.
- Gray ML, Bonventre JV. Training PhD researchers to translate science to clinical medicine: closing the gap from the other side. Nat Med. 2002;8:433-6.
- Archer SL. The making of a physician-scientist the process has a pattern: lessons from the lives of Nobel laureates in medicine and physiology. Eur Heart J. 2007;28:510-4.
- Lazaro A, Gallego-Delgado J, Osende JI, Egido J, Vivanco F. Analysis of antihypertensive drugs in the heart of animal models: a proteomic approach. Methods Mol Biol. 2007;357:45-58.
- Rey M, Valenzuela-Fernández A, Urzainqui A, Yáñez-Mó M, Pérez-Martínez M, Penela P, et al. Myosin II is involved in the endocytosis of CXCR4 induced by SDF-1. J Cell Sci. 2007; 120:1126-33.
- López B, González A, Beaumont J, Querejeta R, Larman M, Díez J. Identification of a potential cardiac antifibrotic mechanism of torasemide in patients with chronic heart failure. J Am Coll Cardiol. 2007;50:859-67.
- de las Heras N, Ruiz-Ortega M, Miana M, Rupérez M, Sanz-Rosa D, Aragoncillo P, et al. Interactions between CTGF and aldosterone in vascular and renal damage in spontaneously hypertensive rats. J Hypertens. 2007;3:629-38.
- González A, Ravassa S, Loperena I, López B, Beaumont J, Querejeta R, et al. Association of depressed cardiac gp130-mediated anti-apoptotic pathways with stimulated cardiomyocyte apoptosis in hypertensive patients with heart failure. J Hypertens. 2007;25:2148-57.
- Ravassa S, González A, López B, Querejeta R, Larman M, Díez J. Upregulation of myocardial annexin A5 is associated with systolic dysfunction in arterial hypertension independently of apoptosis. Eur Heart J 2007;doi:10.1093/eurheartj/ehm370.
- Blanco-Colio LM, Martín-Ventura JL, Muñoz-García B, Orbe J, Páramo JA, et al. Identification of soluble tumor necrosis factor-

like weak inducer of apoptosis (sTWEAK) as a possible biomarker of subclinical atherosclerosis. Arterioscler Thromb Vasc Biol. 2007;27:916-22.

- Corral J, Hernández-Espinosa D, Soria JM, González-Conejero R, Ordoñez A, González-Porras JR, et al. Antithrombin Cambridge II (A384S): an underestimated genetic risk factor for venous thrombosis. Blood. 2007;109:4258-63.
- Verdeguer F, Castro C, Kubicek M, Pla M, Vila-Caballer M, Vinué A, et al. Complement regulation in murine and human hypercholesterolemia and role in the control of macrophage and smooth muscle cell proliferation. Cardiovasc Res. 2007;76: 340-50.
- 15. Serrano H, Jorge I, Martínez-Acedo P, Navarro PJ, Pérez-Hernández D, Miró Casas E, et al. Quantitative proteomics of mitochondrial membrane proteins by sodium dodecyl sulphate polycrylamide gel electrophoresis, 16O/18O stable isotope labeling and linear ion trap mass spectrometry. Proteomica. 2007; 0:29-34.
- Fernandez-Aviles F, Alonso JJ, Pena G, Blanco J, Alonso-Briales J, Lopez-Mesa J, et al. Primary angioplasty vs. early routine postfibrinolysis angioplasty for acute myocardial infarction with STsegment elevation: the GRACIA-2 non-inferiority, randomized, controlled trial. Eur Heart J. 2007;28:949-60.
- Barderas MG, Tunon J, Darde VM, de la Cuesta F, Duran MC, Jimenez-Nacher JJ, et al. Circulating human monocytes in the acute coronary syndrome express a characteristic proteomic profile. J Proteome Res. 2007;6:876-86.
- Mas S, Touboul D, Brunelle A, Aragoncillo P, Egido J, Laprevote O, et al. Lipid cartography of atherosclerotic plaque by cluster-TOF-SIMS imaging. Analyst. 2007;132:24-6.
- Sanchez PL, Santos JL, Kaski JC, Cruz I, Arribas A, Villacorta E, et al; Grupo AORTICA (Grupo de Estudio de la Estenosis Aortica). Relation of circulating C-reactive protein to progression of aortic valve stenosis. Am J Cardiol. 2006;97:90-3.
- San Roman JA, Lopez J, Vilacosta I, Luaces M, Sarria C, Revilla A, et al. Prognostic stratification of patients with left-sided endocarditis determined at admission. Am J Med. 2007;120:e1-7.
- Manzano MC, Vilacosta I, San Román JA, Aragoncillo P, Sarriá C, López D, et al. Síndrome coronario agudo en la endocarditis infecciosa. Rev Esp Cardiol. 2007;60:24-31.
- San Roman JA, Sanz-Ruiz R, Ortega JR, Perez-Paredes M, Rollan MJ, Munoz AC, et al. Safety and predictors of complications with a new accelerated dobutamine stress echocardiography protocol. J Am Soc Echocardiogr. 2007. Available from: http://dx. doi.org/ 10.1016/j.echo.2007.05.025.
- Monserrat L, Hermida-Prieto M, Fernandez X, Rodriguez I, Dumont C, Cazon L, et al. Mutation in the alpha-cardiac actin gene associated with apical hypertrophic cardiomyopathy, left ventricular noncompaction, and septal defects. Eur Heart J. 2007; 28:1953-61.