cnic

SCIENTIFIC REPORT 2025

Go to contents

cnic

SCIENTIFIC REPORT 2025

Go to contents

cnic

SCIENTIFIC REPORT 2025

Fundación pro cnic

cnic

EXCELENCIA SEVERO OCHOA

Go to contents

The Pro CNIC Foundation brings together 11 of the most important Spanish companies and foundations: Acciona, Endesa, Santander Foundation, La Caixa Foundation, MAPFRE Foundation, Mutua Madrileña Foundation, Ramón Areces Foundation, REPSOL Foundation, INDITEX, PRISA and Telefónica.

This innovative public-private financing formula has allowed the CNIC to reach a very high level of excellence, as recognized in the Severo Ochoa accreditation and other international awards.

DL: M-4526-2025

Go to contents

CONTENTS

Back to Contents

1 Foreword and CNIC Mission

The *Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC)* is a leading biomedical research center supported through a pioneering public–private partnership between the Spanish Government and the Pro CNIC Foundation, which comprises eleven Spanish companies outside the biomedical sector. Recognized as a Severo Ochoa Center of Excellence by Spain's Ministry of Science and Innovation since 2011, the CNIC also benefits from the strategic oversight of its international Scientific Advisory Board, which provides guidance on research priorities and recruitment and regularly evaluates institutional and program performance.

Cardiovascular disease (CVD) remains the leading cause of mortality worldwide, and the growing economic and social costs of reactive care continue to place a heavy burden on patients, families, and healthcare systems. To address this challenge, the CNIC pursues three overarching goals: advancing knowledge of cardiovascular health and disease mechanisms, strengthening prevention and health promotion, and accelerating the development of innovative therapies for the most prevalent forms of CVD.

Delivering on these goals requires an integrated research model that combines fundamental and mechanistic studies with translational and clinical research to transform scientific discoveries into more effective strategies for prevention, diagnosis, and patient care. To maximize impact and accelerate knowledge transfer, the CNIC works through strategic collaborations with leading hospitals, universities, and national and international research institutions.

The CNIC's activity is built on four core pillars: excellence in basic and clinical research, advanced technological capabilities, collaborative networks, and educating and training young researchers in the early stages of their careers. Research is organized across two interconnected departments—Basic Research and Clinical Research—and seven integrated programs that cover the full translational continuum from discovery to large-scale clinical studies, while also leveraging the CNIC's strengths in cutting-edge technologies, advanced imaging, preclinical models, and data science.

A major institutional achievement in 2025 was the center's success in securing competitive funding from national and international sources. Among the international awards obtained were three European Research Council (ERC) Advanced Grants and two Innovative Health Initiative projects, reinforcing the CNIC's contribution to major international scientific initiatives. At the national level, CNIC researchers secured several highly competitive awards, including coordinator roles on two "la Caixa" Health Research projects.

Publications last year by CNIC researchers in leading international journals provided important mechanistic insights into cardiovascular physiopathology, further consolidating the center's position at the forefront of basic cardiovascular research, including significant contributions to the field of rare diseases featuring cardiovascular involvement. The year also delivered significant translational impact. One of the most notable milestones was the publication of the main results of two CNIC-coordinated trial, REBOOT-CNIC and DPATAVI, in The New England Journal of Medicine and one in The Lancet. The REBOOT-CNIC trial challenged a clinical practice that had remained largely unchanged for more than four decades in the management of myocardial infarction. The study achieved broad international visibility, generating media coverage across 31 countries and 11 languages and reaching an estimated audience close to one billion people.

The CNIC also played a prominent role at the ESC Congress 2025, held in Madrid from 29 August to 1 September. One of the world's leading meetings in cardiovascular medicine, the congress convened researchers, clinicians, and healthcare professionals to discuss the latest advances in cardiovascular science and clinical practice. CNIC researchers contributed extensively through invited lectures, guideline and consensus sessions, presentations of clinical findings, and participation in high-level scientific discussions. This strong scientific presence reinforced the CNIC's position as a leading international center and underscored its commitment to generating knowledge that advances prevention, diagnosis, and treatment through the integration of basic, translational, and clinical research. The CNIC also led the publication of the first guideline document on mental health and cardiovascular disease.

Further achievements from 2025 are detailed throughout this report. As we look ahead, the CNIC remains committed to excellence, innovation, and collaboration across disciplines. By integrating basic and clinical research, the center will continue to generate high-impact discoveries and train the next generation of scientists to reduce the global burden of cardiovascular disease.

Valentín Fuster, General Director
Borja Ibáñez, Scientific Director and Clinical Research Director
Vicente Andrés, Basic Research Director

Madrid, July 2026


cniic

2 Research at the CNIC

Back to Contents

Scientific Programs

1 Novel Mechanisms of Atherosclerosis

Coordinator: José Javier Fuster
Clinical Leaders: Valentín Fuster & Inés García-Lunar

The Novel Mechanisms of Atherosclerosis Program aims to advance our mechanistic understanding of atherosclerosis, the leading cause of cardiovascular and cerebrovascular disease. Despite major progress in controlling traditional risk factors, a substantial residual risk of atherosclerotic cardiovascular disease persists, even in individuals with low estimated cardiovascular risk. A central goal of the Program is therefore the identification of new risk factors and mechanisms of atherosclerosis in order to develop novel strategies for the prediction, prevention and treatment of atherosclerosis.

To achieve this, the Program brings together multidisciplinary teams, integrating experimental studies in animal models with translational research in humans, leveraging large cohorts such as the Progression of Early Subclinical Atherosclerosis (PESA) study. Research efforts focus on inflammatory mechanisms, vascular cell biology, and novel imaging and molecular biomarkers of atherosclerosis.

Key Achievements in 2025

A microbiota metabolite–receptor axis as a new therapeutic opportunity. A major advance was the identification of imidazole propionate (ImP) as a microbial metabolite linked to the development of atherosclerosis in mice and humans. The study, published in *Nature (1)*, also identified the imidazoline 1 receptor in myeloid cells as the sensing receptor mediating ImP-induced proinflammatory reprogramming and accelerated atherosclerosis development. The translational relevance of these findings was reinforced by associations with active atherosclerosis in human cohorts, including PESA. Pharmacological blockade of the ImP-sensing pathway prevented atherosclerosis in mice.

Targeting dendritic cell–driven adaptive immunity to slow disease progression. Program researchers identified conventional type 1 dendritic cells (cDC1s) as key orchestrators of adaptive immune responses promoting atherosclerosis. This work, published in *Circulation Research (2)*, showed that cDC1s regulate local Th1 immunity within atherosclerotic plaques and play a causal role in disease progression. Importantly, it also provided a new preventive strategy: dexamethasone-loaded nanoparticles targeted to cDC1s suppressed plaque Th1 immunity and prevented atherosclerosis progression in experimental models.

Mechanistic understanding of imaging-based stratification and treatment monitoring strategies. Imaging with the radiolabeled glucose analog fluorodeoxyglucose (FDG) is widely used to monitor atherosclerosis in clinical trials, but the cellular and molecular processes underlying FDG uptake in the vascular wall remain incompletely defined. Using a large-animal model of atherosclerosis, program researchers showed that atherosclerotic disease activity correlates with glycolytic enzyme expression across multiple plaque cell types, which in turn correlates with vascular FDG uptake. Published in *Science Translational Medicine (3)*, these findings provide a mechanistic rationale for FDG uptake as a readout of plaque activity, linking this imaging signal to glycolytic programs in vascular and immune cells within the lesion.

Funding and awards

A major milestone in 2025 was the award of an ERC Advanced Grant to Almudena R. Ramiro, reinforcing CNIC's leadership in immune mechanisms of atherosclerosis. In addition, Vicente Andrés' group received the Best Publication Award *(1ª Edición Premios Cátedra Enfermedades Poco Frecuentes, Universidad de Almería)* for prior work within the Program describing the contribution of endothelial-to-mesenchymal transition to accelerated atherosclerosis in Hutchinson–Gilford progeria syndrome.

Outreach and engagement

Program researchers presented findings at major international meetings, including ESC, AHA Vascular Discovery, Gordon Conferences, Keystone Symposia, EMBO workshops, ESC Cardio-Oncology, ESC Heart Failure Congress, and CARDIOTOX, with invited lectures by group leaders and presentations by early-stage investigators. David Sancho co-organized the European Phagocyte Workshop 2025 at the CNIC.

Public engagement activities included participation in the European Researchers' Night, Madrid Science Week, the International Day of Women and Girls in Science, the International Day of Persons with Disabilities, and educational activities in primary and secondary schools across the Comunidad de Madrid.

Highlighted Publications

1. Nature 2025 Sep;645(8079):254-261. doi: 10.1038/s41586-025-09263-w
2. Circ Res. 2025 Jul 18;137(3):400-416. doi: 10.1161/CIRCRESAHA.124.325792
3. Sci Transl Med. 2025 Aug 13;17(811):eado6467. doi: 10.1126/scitranslmed.ado6467
4. Arterioscler Thromb Vasc Biol. 2025 Sep;45(9):1616-1635.doi: 10.1161/ATVBAHA.124.322893
5. Arterioscler Thromb Vasc Biol. Epub 2025 Dec 23;46(2):e323323. doi: 10.1161/ATVBAHA.125.323323
6. Nat Commun. 2025 Apr 9;16(1):3369. doi: 10.1038/s41467-025-58289-1
7. Immunity. 2025 Feb 11;58(2):381-396.e9. doi: 10.1016/j.immuni.2024.12.012

RESEARCH GROUPS

Vicente Andrés
Molecular and Genetic Cardiovascular Pathophysiology

Jacob Fog Bentzon
Experimental Pathology of Atherosclerosis

Miguel Ángel del Pozo
Mechanoadaptation and Caveolae Biology

José Javier Fuster
Hematovascular Pathophysiology

Valentín Fuster
Cardiovascular Imaging and Population Studies

Inés García Lunar
Cardiovascular Prevention Through Non-Invasive Imaging

Carlos Pérez-Medina
Nanomedicine and Molecular Imaging

Almudena R. Ramiro
B Lymphocyte Biology

Fátima Sánchez-Cabo
Computational Systems Biomedicine

David Sancho
Immunobiology

Jesús Vázquez
Cardiovascular Proteomics

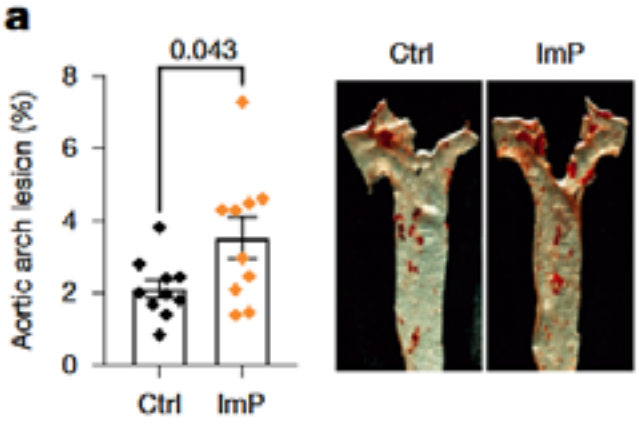


Fig 1.
Imidazole propionate promotes aortic atherosclerosis i**n ApoE-deficient mice, an effect prevented by AGN192403.** Lesion area in the aortic arch was quantified by Oil Red O staining (left), with representative images shown on the right. Mastrangelo A, Robles-Vera I et al, *Nature* 2025.

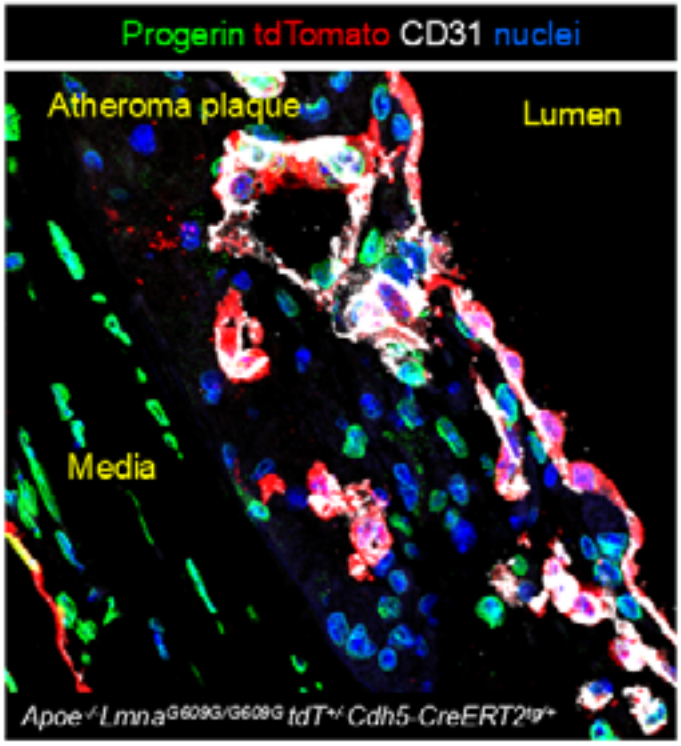


Fig 2.
Lineage tracing reveals the abnormal presence of endothelial-derived cells within the atheroma of progeroid, atherosclerosis-prone tdT+/- Cdh5-CreERT2 tg/+ mice. Representative immunofluorescent image.

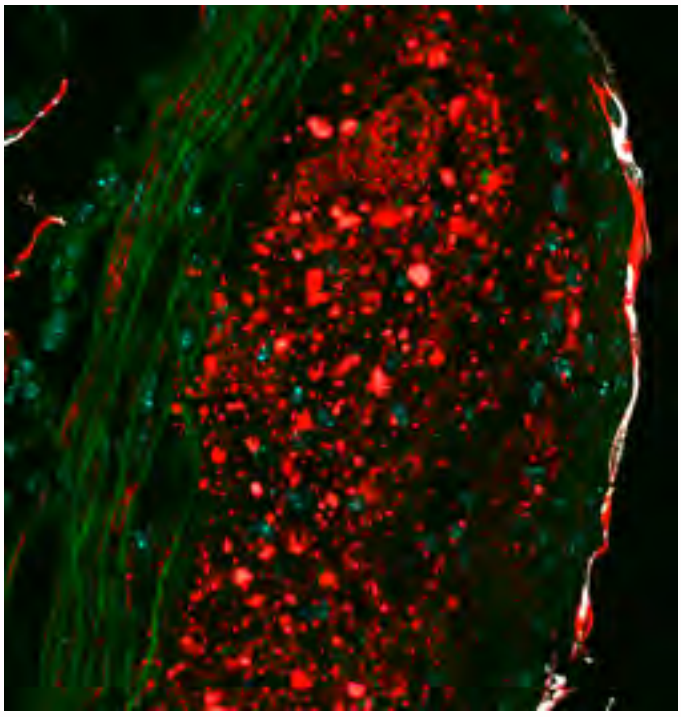


Fig 3.
Endothelial and medial CAV1 expression during atherogenesis. Representative immunofluorescence image of the left coronary sinus showing CD31 (white), CAV1 (red), and nuclei (blue) in hypercholesterolemic mice. Muñiz-Anquela et al, ATVB Epub 2025 Dec 23.

2 Myocardial Homeostasis and Cardiac Injury (MERCURY)

Back to Contents

Coordinator: Enrique Lara-Pezzi
Clinical Leader: Borja Ibáñez

The MERCURY program investigates the molecular, genetic, and physiological mechanisms that determine how the heart responds to stress, injury, and inherited disease, with the aim of developing more precise and effective therapies.
In 2025, the program continued to explore two complementary research areas:

(i) cardiotoxicity induced by cancer therapies and systemic stress, and
(ii) the genetic and molecular basis of inherited cardiomyopathies, with a strong focus on translational and gene-based therapies

Key Achievements in 2025

Cardiotoxicity and cardiac vulnerability
During 2025, we continued to explore cardiotoxicity as a context-dependent process influenced by metabolic state and genetic background. Using integrated approaches combining mouse models, large animal studies, and clinical research, we re-examined long-standing assumptions in cardiovascular therapy and cardioprotection.

Results from the REBOOT randomized clinical trial and a complementary meta-analysis (1, 2) showed that chronic beta-blocker therapy is not required in many post–myocardial infarction patients with preserved cardiac function. In parallel, studies in large-animal models demonstrated that subclinical metabolic alterations can increase susceptibility to chemotherapy-induced cardiac injury, even at doses traditionally considered safe. Together, these findings provide a framework for improved risk stratification and for preventive strategies tailored to individual metabolic profiles.

Sarcomere mechanics and structural integrity
We also made progress in understanding how force transmission is maintained in striated muscle. We found that loss of mechanical tension across the giant protein titin — caused either by proteolytic cleavage or post-translational modification — disrupts cardiomyocyte adhesion and promotes myocardial fibrosis.

Using single-molecule approaches applied to native titin, including the study of modifications induced by glycative stress, we identified new links between metabolic stress, sarcomeric mechanics, and pathological remodeling. These results connect mechanisms of cardiac and skeletal muscle disease and suggest new therapeutic strategies aimed at preserving force transmission and tissue integrity.

Inherited cardiomyopathies: clinical and molecular studies
The second pillar of the program focused on inherited cardiomyopathies and yielded several major advances in 2025.

At the clinical level, we helped define how genetic subtype influences disease progression, complications, and treatment response in hypertrophic and dilated cardiomyopathies. We completed a left–right ventricular differential expression study using myocardial samples from patients with pathogenic mutations who required heart transplantation, providing direct evidence of chamber-specific molecular programs in advanced disease.

In addition, results of the MAPLE-HCM study established a new therapeutic paradigm for obstructive hypertrophic cardiomyopathy, showing that genotype-guided strategies can directly improve patient management.

Gene-based therapies for cardiomyopathy
We made important progress in the development of gene-based therapies for inherited cardiac disease. In a model of severe arrhythmogenic cardiomyopathy, adeno-associated virus–mediated overexpression of wild-type TMEM43 improved cardiac function, electrical stability, fibrosis, and survival. Both preventive and therapeutic administration were effective, demonstrating that dominant cardiomyopathies can be treated by restoring protein balance rather than silencing mutant alleles.

We also provided the first in vivo demonstration that CRISPR-based transcriptional activation can correct electrical defects caused by haploinsufficient truncating variants that cannot be treated by conventional gene replacement. Activation of endogenous gene expression using compact AAV-delivered CRISPRa systems reversed arrhythmogenic phenotypes in adult animals, opening a new therapeutic approach for a broad class of inherited cardiac diseases.

Precision modeling and variant interpretation
To support next-generation gene therapy, we established an integrated computational–experimental framework for the analysis of arrhythmogenic cardiomyopathy variants. Focusing on PKP2, the most frequently affected gene in this disease, we generated and analyzed hundreds of structural models of clinically annotated variants using artificial-intelligence–based methods.

These models allow systematic classification of pathogenic mechanisms and predicted functional behavior, strengthening the link between genetic diagnosis and therapeutic design, and enabling the development of mutation-aware gene therapy vectors.

Together, these advances support a unified view of cardiac disease as the result of dynamic interactions between genetic background, molecular regulation, and systemic context, and demonstrate the feasibility of mechanism-based, genetically informed strategies.

Awards and Recognition

- Agustín Clemente Moragón received the CNIC Award for Outstanding Doctoral Thesis.
- Results from highlighted publications 1-3 were presented in plenary sessions at the European Society of Cardiology Congress 2025 (Madrid) and received broad media coverage.
- Biophysical Society — Michael and Kate Bárány Award (2026)

Highlighted Publications

1. N Engl J Med. 2025 Nov 13;393(19):1889-1900. doi: 10.1056/NEJMoa2504735
2. N Engl J Med. Epub Nov 9, 2025. 394(6):540-55 (2026) doi: 10.1056/NEJMoa2512686
3. N Engl J Med. 2025 Sep 11;393(10):949-960. doi: 10.1056/NEJMoa2504654
4. Eur Heart J. 2025 Nov 14;46(43):4610-4613. doi: 10.1093/eurheartj/ehaf703
5. Nat Biomed Eng. 2025 Oct;9(10):1758-1774. doi: 10.1038/s41551-025-01403-x

RESEARCH GROUPS

Jorge Alegre-Cebollada
Molecular Mechanics of the Cardiovascular System

Ana Devesa
Cardiometabolic Disease and Advanced Imaging

Ana García Álvarez
Heart Failure and Pulmonary Hypertension Translational Research

Pablo García-Pavía
Inherited Cardiomyopathies

Borja Ibáñez
Translational Laboratory for Cardiovascular Imaging and Therapy

Enrique Lara-Pezzi
Molecular Regulation of Heart Failure

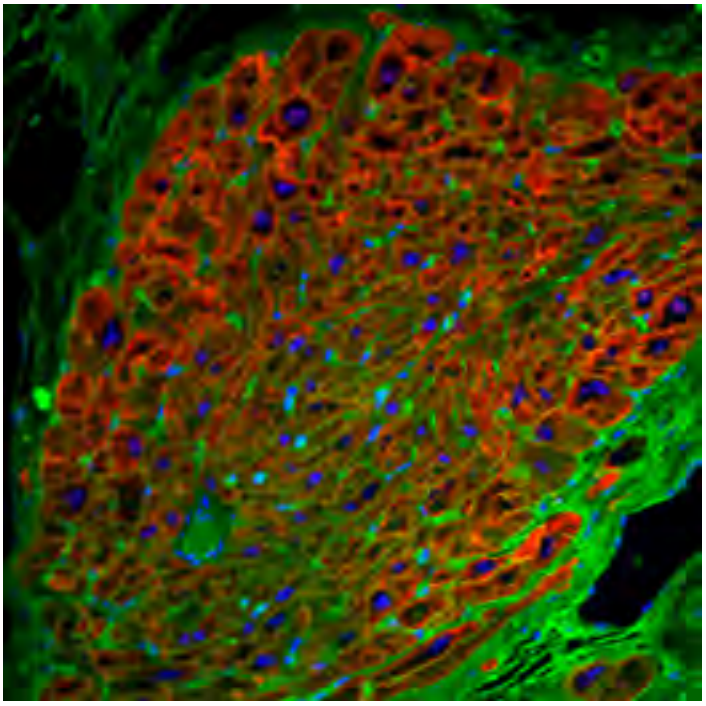


Fig 1.
Immunofluorescence analysis of a myocardial sample from a hypertrophic cardiomyopathy patient. Blue, DAPI; Green, agglutinin; Red, troponin.

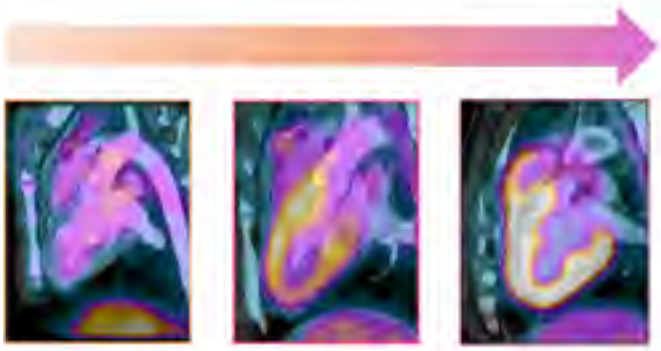


Fig 2.
PET scan during cardiotoxicity development showing abnormal glucose metabolism with a prior hypertensive stimulus.

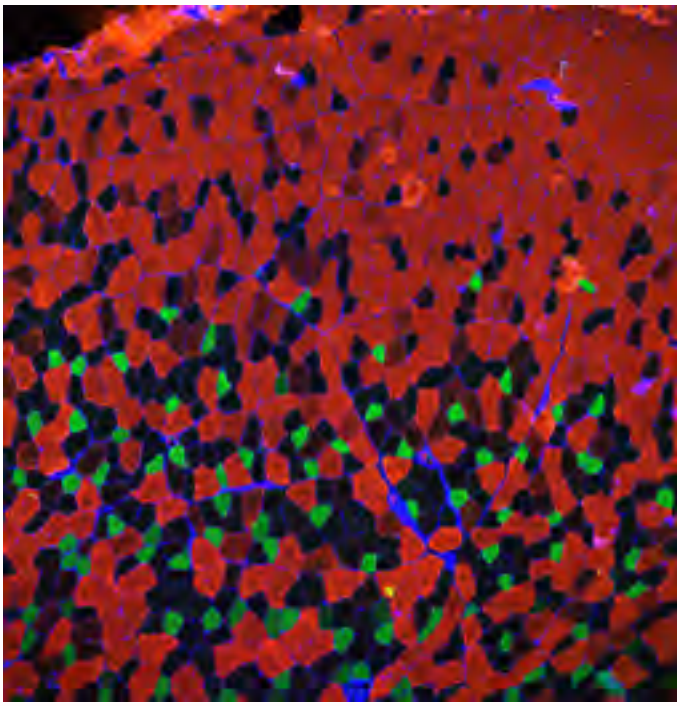


Fig 3.
A cross section of mouse skeletal muscle stained to distinguish different types of muscle cells.

3 Cardiovascular Regeneration

Back to Contents

Coordinator: Miguel Torres
Clinical Leader: Hesham Sadek

The Cardiovascular Regeneration Program **(CVRP)** investigates the fundamental mechanisms governing cardiovascular development, injury, and regeneration, with the goal of translating this knowledge into therapeutic strategies for cardiovascular disease.

In 2025, the program advanced understanding of the cardiac response to injury and generated new experimental tools and therapeutic approaches.

Key Achievements in 2025

Metabolic Regulation of Cardiac Function

- ***Conscore—A conservation-based framework for the analysis of mitochondrial energy production:*** Jose Antonio Enríquez's group developed *ConScore*, a conservation-based tool that predicts the pathogenicity of mutations associated with oxidative phosphorylation (OxPhos). Using this approach, they mapped the coevolution of the 103 OxPhos protein subunits, identifying key constraints that ensure proper function. This unified framework integrates structural biology, population genetics, and evolutionary analysis, improving detection of clinically relevant genetic variants and deepening understanding of the architecture, adaptability, and pathogenic potential of the mitochondrial energy production system (1).

Heart Injury and Regeneration

- ***Paternal influences on offspring response to cardiac injury:*** Following cardiac injury, systemic stress can alter the function of remote organs. Whether such stress affects gametogenesis and transmits heritable changes to subsequent generations remains unclear. Using a mouse model, the Mercader group showed that offspring of males subjected to cardiac cryoinjury during early postnatal life exhibit enhanced transient ventricular plasticity and improved LV compliance (2).

- ***Resetting the body clock to improve outcome after myocardial infarction***: The Hidalgo lab identified a mechanism by which circadian oscillations confer time-of-day-dependent cardioprotection through the redistribution of neutrophils away from the healthy tissues. They further identified a pharmacological intervention capable of modulating this immune timing to align with periods of maximal protection (8).

- ***Activating cardiomyocytes to boost cardiac regeneration***: The Torres lab demonstrated that induced Myc expression at homeostatic levels induces partial dedifferentiation of adult mouse cardiomyocytes, increasing their proliferative capacity and improving functional recovery after myocardial infarction (4).

- ***Forced activation of cardiomyocyte proliferation improves cardiac function:*** The Sadek lab showed that temporally regulated overexpression of pro-cytokinetic factors in the adult heart induces cardiomyocyte proliferation and enhances left ventricular systolic function after myocardial infarction (3).

- ***A secreted factor that induces heart regeneration:*** The Sadek lab also identified the paracrine factor Igfbp3 as a secreted molecule induced in the neonatal heart after injury that mediates regenerative responses. Forced expression of Ipfbp3 in the adult heart promotes cardiomyocyte proliferation and improves functional recovery after injury (J Mol Cell Cardiol, 2025).

Mechanistic Studies in Heart Disease and Tissue Repair

- ***Cellular mechanisms underlying skin barrier protection:*** The Hidalgo lab identified a population of immune cells in the skin that contribute to tissue repair, protection, and fibrotic responses (9).

- ***Signals that disturb cardiac electrical conduction:*** Jose Luis de la Pompa's group discovered signaling mechanisms that control ventricular wall and conduction system maturation and are linked to cardiomyopathy (PLoS One 2025). The group has also advanced the characterization of novel genes involved in ventricular development and heart disease.

Cardiovascular Development

- ***A revised cellular map of heart development:*** Miguel Torres and colleagues used single-cell live tracking and prospective lineage labelling to redefine the origins of the cell populations that form the heart and to map their interactions during mammalian embryogenesis (5).

- ***Lymphatic vessels find their niche in the epicardium:*** The Torres lab identified epicardial signals required for coronary lymphangiogenesis, establishing the sub-epicardium as a critical niche for cardiac lymphatic vessel development (6).

Experimental therapies in model organisms

- ***Retuning cardiac rhythm:*** José Jalife and colleagues showed that treatment with the polyamines spermine or spermidine restores normal cardiac electrical activity and reduces arrhythmia susceptibility in a mouse model of Short QT Syndrome type 3 (SQTS3). Polyamines corrected potassium channel dysfunction and improved sodium channel function, supporting their potential as a therapeutic strategy for SQTS3-related arrhythmias (bioRxiv, 2025).

- ***Repurposing risedronate for genetic cardiomyopathy:*** Hesham Sadek's group used virtual docking to identify risedronate, an FDA-approved drug, as a candidate therapy able to structurally and functionally correct the sarcomeric troponinT K210del mutation in mice and human IPSC-derived cardiomyocytes (7).

Awards and Recognition

- Miguel Torres was awarded **The National Prize in Genetics** from the Spanish Society of Genetics in July 2025.

Highlighted Grants in 2025

- **Advanced ERC Grant**. José Antonio Enríquez was awarded 2.5€ million for the project MINTRAF: Cell-Cell Communication by Mitochondrial Intercellular Traffic (2025-2030).

- **Horizon Europe EIC Pathfinder Grant**. Florian Weinberger was awarded €690,000 for the project HEARTVISION: ILLUMINATING NEW PATHS IN HEART FAILURE THERAPY (2026-2030).
- **ERA4Health**. Hesham Sadek was awarded €175,000 as part of the multi-investigator FONTANA project to develop novel therapeutics for myocardial regeneration (2025-2028).

Highlighted Publications

1. Cell Genom. 2025 Sep 10;5(9):100945. doi: 10.1016/j.xgen.2025.100945
2. Circulation. 2025 Apr;151(13):968-971. doi: 10.1161/CIRCULATIONAHA.124.070323
3. Circulation. 2025 Apr 8;151(14):1009-1023. doi: 10.1161/CIRCULATIONAHA.124.065763
4. J Mol Cell Cardiol. 2025 Oct:207:93-106. doi: 10.1016/j.yjmcc.2025.08.004
5. Commun Biol. 2025 Jul 18;8(1):1069. doi: 10.1038/s42003-025-08360-w
6. Dev. Cell. 2025 Sep 22;60(18):2434-2444.e5. doi: 10.1016/j.devcel.2025.05.002
7. EMBO Reports 2025 Jun;26(11):2803-2818. doi: 10.1038/s44319-025-00431-7
8. J Clin Invest. 2025 Feb 17;135(4):e174081. doi: 10.1172/JCI174081
9. J Exp Med. 2026 Feb 2;223(2):e20250240. doi: 10.1084/jem.20250240
10. Nature. 2025 May;641(8063):740-748. doi: 10.1038/s41586-025-08741-5

RESEARCH GROUPS

Rui Benedito
Molecular Genetics of Angiogenesis

José Luis de la Pompa
Intercellular Signaling in Cardiovascular Development and Disease

José Antonio Enríquez
Functional Genetics of the Oxidative Phosphorilation System (GENOPHOS)

Andrés Hidalgo
Imaging the Cardiovascular Inflammation and the Immune Response

José Jalife
Cardiac Arrhythmia

Nadia Mercader
Development of the Epicardium and its Role during Regeneration

Hesham Sadek
Myocardial Regeneration via Cardiomyocyte Cell Cycle Regulation

Miguel Torres
Genetic Control of Organ Development and Regeneration

Florian Weinberger
Cardiac Tissue Engineering and Regenerative Therapies

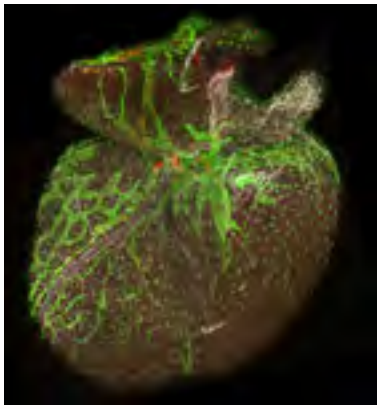


Fig 1.
A late fetal mouse heart, showing the coronary lymphatic vasculature in green+red, macrophages in green, and coronary veins in gray.

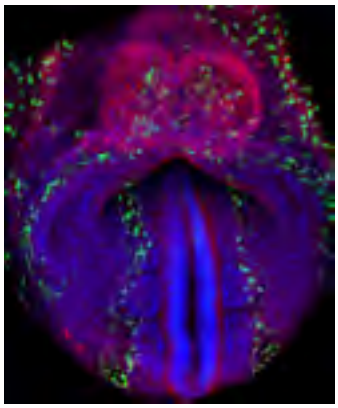


Fig2.
The developing heart of an E8 mouse embryo, showing myocardium in red and endothelial cells in green.y.

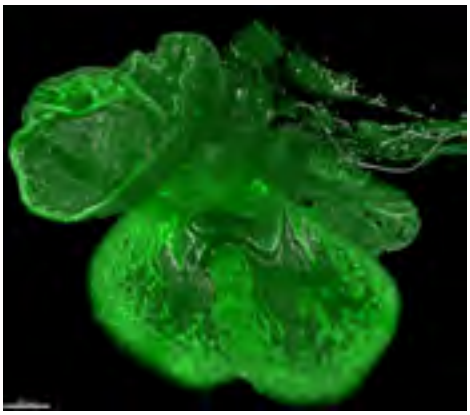


Fig3.
3D reconstruction of an E13.5 wild-type heart, transverse view. The myocardium (green) is labeled with Tnnt2 and the endocardium (white) with Iso-lectin-B4. Note the trabeculae extending toward the ventricular lumen.

4 Novel Arrhythmogenic Mechanisms

Coordinator: Silvia Priori
Clinical Leader: David Filgueiras

The Novel Arrhythmogenic Mechanisms program investigates the cellular, molecular, and electrophysiological processes that lead to cardiac arrhythmias, with the aim of identifying new therapeutic targets and improving the prevention and treatment of life-threatening rhythm disorders. The program combines experimental models, computational approaches, and translational studies to understand both rare inherited channelopathies and common arrhythmias associated with structural heart disease.

In 2025, the program made advances in three main areas: calcium-handling disorders, gene-based therapies for inherited channelopathies, and the identification of electrophysiological substrates responsible for ventricular arrhythmias.

Disruption of intracellular calcium regulation
Research during the past year focused on the consequences of defective calcium handling using a mouse model of Triadin-knockout syndrome, a recessive inherited disorder characterized by severe arrhythmias caused by the absence of Triadin, a protein essential for the organization of cardiac Ca^{+2} release complexes.

We found that Ca^{+2} handling proteins in Triadin-deficient hearts fail to localize correctly to Ca^{+2} release units and are instead degraded through aggrephagy and lysosomal pathways. These findings explain the reduced expression of Ca^{+2} handling proteins previously reported in this disease.

Structural studies confirmed that Ca^{+2} release complexes are severely disorganized in Triadin-knockout hearts. Introduction of either Triadin itself or the structural protein Junctophilin 2 in affected animals restored normal ultrastructure and significantly improved the arrhythmic phenotype, demonstrating that correction of structural defects can reverse the functional consequences of the disease (Figure 1).

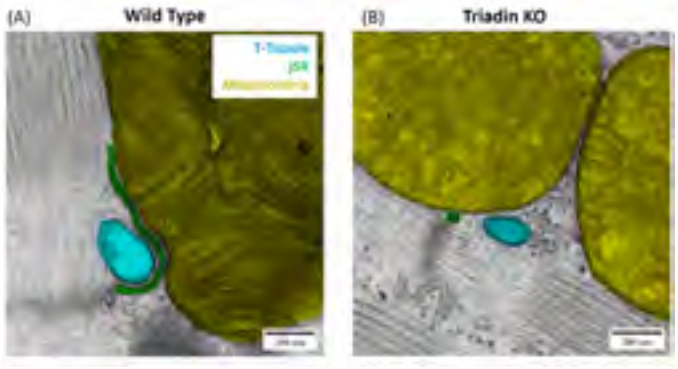


Fig 1. Transmission electron microscopy micrographs of cardiac Ca^{+2} release units and associated mitochondria. (A) Wild-type hearts show normal association between T-tubules, junctional sarcoplasmic reticulum (jSR), and mitochondria, whereas Triadin-knockout hearts display marked structural disorganization—with T-tubule and jSR shrinkage and separation—associated with abnormal Ca^{+2} handling.

New targets and gene therapies for inherited channelopathies
A second line of work focused on the development of new therapies for inherited channelopathies, with particular attention to Timothy Syndrome type 1, a severe arrhythmogenic disorder with very poor survival in affected patients.

In collaboration with the Molecular Cardiology laboratory at IRCCS Maugeri and the University of Pavia, we developed a gene-therapy approach for Timothy syndrome and tested it in knock-in swine carrying the disease mutation. Treatment improved the electrical phenotype in vivo, providing proof of principle that gene therapy can correct this disorder.

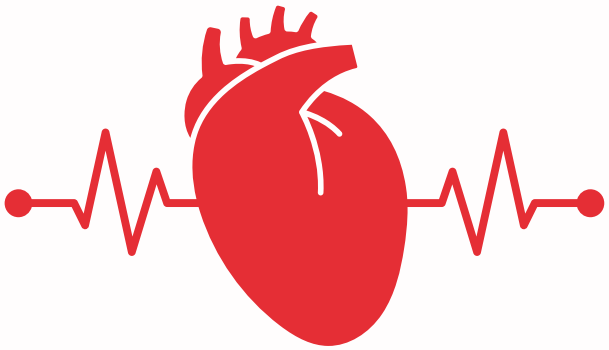
Computational studies performed in collaboration with the University of Pavia generated in-silico models of cardiomyocytes derived from induced pluripotent stem cells, allowing detailed analysis of the electrophysiological alterations associated with Timothy syndrome (in press). Ongoing work is evaluating the gene therapy strategy in human iPSC-derived cardiomyocytes to assess its translational potential.

Electrophysiological substrates of ventricular arrhythmias
The program also continued long-standing work aimed at identifying the myocardial substrate responsible for ventricular arrhythmias in ischemic cardiomyopathy.

Using single-beat multipolar recordings obtained during programmed ventricular stimulation, we showed that regions with large activation-time dispersion reliably identify protected isthmus sites responsible for infarct-related monomorphic ventricular tachycardia (Figure 2). Increasing degrees of activation-time dispersion were associated with progressively more severe post-stimulation outcomes, ranging from non-inducible arrhythmia to ventricular fibrillation. Although obtained in experimental models, these findings can be translated to clinical practice using already available mapping tools.

Additional studies examined the electrophysiological and structural mechanisms that determine ventricular fibrillation dynamics. We identified interventricular differences in endocardial and epicardial activation rates during both short and prolonged episodes of fibrillation, reflecting unequal tolerance to global ischemia. Similar activation-rate patterns were observed in surface ECG recordings from patients, where higher activation rates were associated with poor neurological outcomes. The results indicate that ventricular activation rate during fibrillation may serve as a dynamic marker of ischemia damage in both the heart and other vital organs.

Training, Meetings, and Recognition
Program researchers participated in major international meetings, including the ESC, EHRA, and EWGCCE conferences. Ana Simón-Chica received the Outstanding Thesis Dissertation Award from the Universidad Carlos III (Madrid).



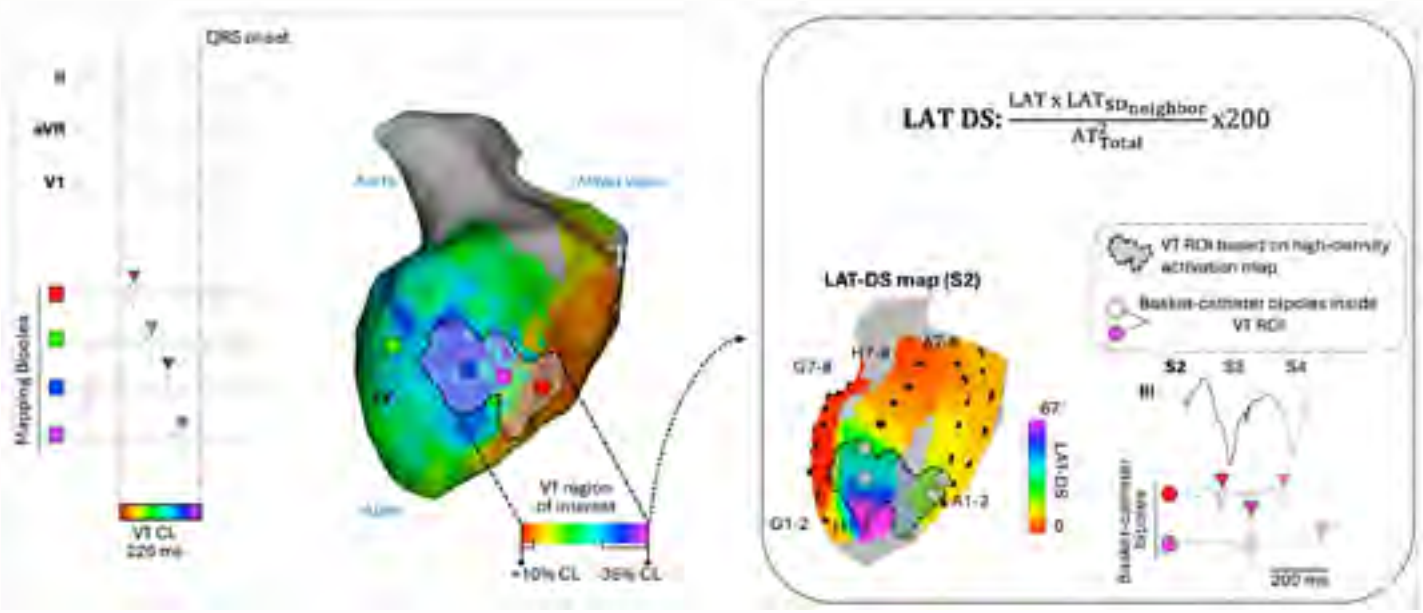


Fig 2. Electrophysiological mapping of ventricular tachycardia (VT) circuits in a heart with infarct-related scarring. Left, Three surface ECG leads during VT and sample electrograms at different mapping locations on the color-coded high-density activation map. On the map, the VT region of interest (ROI), containing the critical site for VT maintenance (isthmus site) is demarcated with a black dashed line.

Right, The VT isthmus site is identified on the local activation time dispersion score (LAT-DS) map of the first coupled extra-stimulus (S2) of the programmed ventricular stimulation prior to VT induction. Basket-catheter bipoles inside the VT ROI are highlighted with gray and purple circles. Sample electrograms are also shown from basket catheter bipoles inside (purple) and outside (red) the VT ROI.

Highlighted Publications and Conference Presentations

1. Eur Heart J. 2025 Nov; 46(Supplement 1). doi: 10.1093/eurheartj/ehaf784.4747
2. Sci Rep. 2026 Feb 16;16(1):9260. doi: 10.1038/s41598-026-37707-4
3. European Society of Cardiology, 2025 Congress. Late-Breaking Basic & Translational Science Session. Treating Timothy Syndrome.

RESEARCH GROUPS

David Filgueiras
Advanced Development in Arrhythmia Mechanisms and Therapy

Silvia Priori
Molecular Cardiology

5 Cardiovascular Risk Factors and Brain Health

Coordinator: María Ángeles Moro
Clinical Leader: Valentín Fuster

The Cardiovascular Risk Factors and Brain Health program investigates the bidirectional relationship between cardiovascular disease and neurological disorders, with particular emphasis on stroke, Alzheimer's disease, vascular cognitive impairment, immune–metabolic interactions, and mental health. The program integrates vascular biology, immunology, neuroinflammation, translational stroke research, cardiovascular prevention, and clinical consensus development to advance mechanistic understanding and therapeutic innovation.

In 2025, the program made major advances in the study of the heart-brain axis, combining conceptual work, translational studies, imaging innovation, and international clinical initiatives that were reflected in publications in leading journals. The program's collective contributions reinforced the view of cardiovascular disease as a systemic condition with critical neurological consequences and identified immune and thrombo-inflammatory pathways as actionable therapeutic targets.

Key Achievements in 2025

The heart–brain–metabolism axis

A major conceptual milestone was the publication of a review in the *Journal of the American College of Cardiology* (Tardo et al., 2025)—with key contributions from program members Valentín Fuster and Marta Cortes-Canteli—defining the heart–brain–metabolism axis as a unifying framework linking cardiometabolic dysfunction with neurodegeneration and cognitive decline **(Fig. 1)**. This review brought together evidence showing that cardiovascular and neurological diseases share inflammatory, thrombo-inflammatory, and metabolic pathways, providing a roadmap for integrated therapeutic strategies.

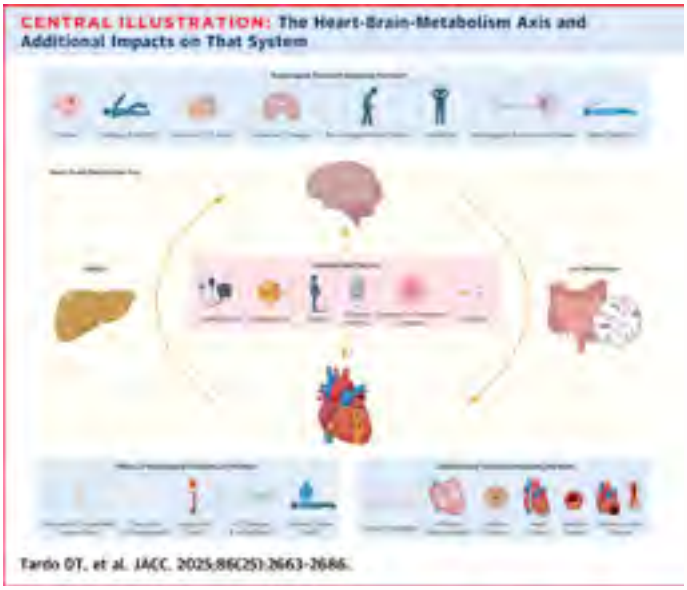


Fig 1.
The heart-brain-metabolism axis and additional impacts on that system.

Stroke, inflammation, and trained immunity

Stroke research remained a central pillar of the program. A perspective article in *Stroke* (5) highlighted innate immune memory as a modifiable determinant of stroke susceptibility and outcome, positioning trained immunity as a target for prevention **(Fig. 2)**.

Fig 2.
The role of innate immune memory in stroke risk and outcome.

Translational work from María Ángeles Moro's group (Stroke, 2025) further showed that daytime DNase-I administration protects mice from ischemic stroke without increasing haemorrhagic risk, even in the presence of aspirin, supporting the safety of therapeutic strategies targeting neutrophil extracellular traps (NETs).

Complementary studies from Hector Bueno's group characterized NETs in acute myocardial infarction, strengthening the mechanistic link between thrombosis, inflammation, and ischemic injury (J Cardiovasc Transl Res, 2025). In addition, María Ángeles Moro's participation in a Leducq-funded multicenter collaboration bore fruit in methodological recommendations to standardize post-stroke cognitive assessment in preclinical models, improving reproducibility and translational alignment (J Cereb Blood Flow Metab, 2025).

Vascular mechanisms in Alzheimer's disease

Program scientists also advanced the vascular dimension of Alzheimer's disease. A review from Marta Cortes-Canteli (Curr Opin Cell Biol, 2025) consolidated evidence that Alzheimer's disease involves a procoagulant and vascular dysfunction component, reinforcing the concept of the disease as a thrombo-inflammatory disorder.

In parallel, new brain-penetrant peptide and antibody radioligands were developed to enable PET imaging of fibrin, providing a translational tool to visualize vascular pathology in vivo (EJNMMI Radiopharm Chem, 2025).

Mental health and cardiovascular disease

Mental health and cardiovascular disease constituted another strategic area of activity. The 2025 ESC Clinical Consensus Statement on mental health and cardiovascular disease (Eur Heart J, 2025) represented a major international effort integrating psychiatric and cardiovascular care **(Fig. 3)**. Additional work explored the relationship between depression, seasonal patterns, and cardiovascular risk, highlighting the importance of psychosocial determinants of cardiovascular outcomes (Eur J Prev Cardiol, 2025).

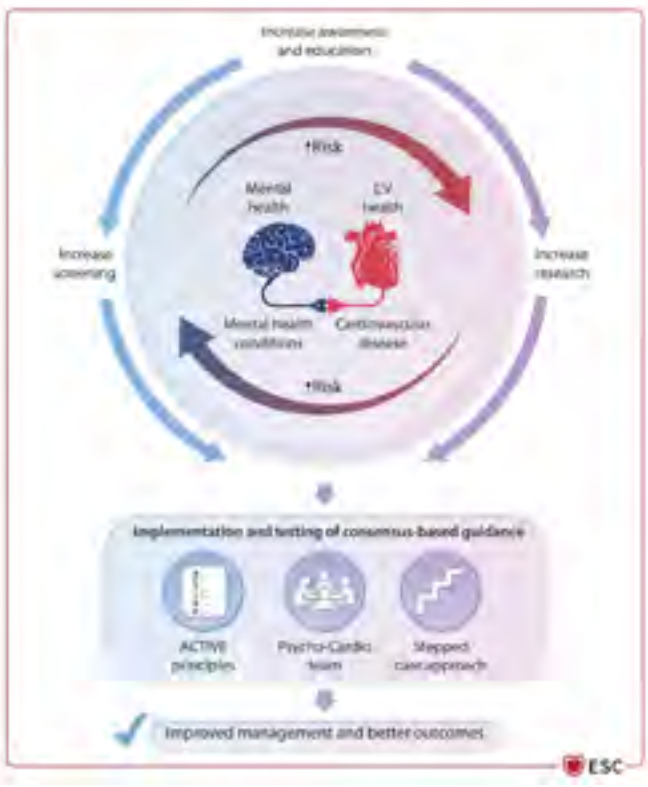


Fig 3.
Mental/cardiovascular health, disease interaction, and future directions. (CV: cardiovascular. ACTIVE: **A**cknowledge, **C**heck, (use validated) **T**ools, **I**mplement, **V**enture, **E**valuate).

Immune–vascular interactions in cardiovascular disease

The program also contributed to broader immunocardiovascular research. A comprehensive review in the *Journal of Clinical Investigation*, authored by Pilar Martín with Francisco Sánchez-Madrid (J Clin Invest, 2025), examined the role of T cells in cardiac health and disease, advancing understanding of adaptive immunity in cardiovascular pathology. An additional study explored systemic immune–vascular interactions in cardio-oncology showing how peripheral ischemia induces myeloid-skewed hematopoiesis and systemic immune remodeling, underscoring the impact of vascular stress on innate immune regulation and inflammatory responses (JACC CardioOncol, 2025).

Awards and Recognition

In 2025, several program members received national and international awards and fellowships, including the *Alumna Illustris* distinction form the Universidad de Alcalá School of Pharmacy to María Ángeles Moro, MSCA postdoctoral fellowships, regional predoctoral contracts, and young investigator awards from the Spanish Society of Biochemistry and Molecular Biology and the European Society of Cardiology.

Highlighted Publications

Original Articles

1. Rev Esp Cardiol (Engl Ed). Epub Sep 19, 2025. 79(3):247-256 (2026). doi: 10.1016/j.rec.2025.08.005
2. N Engl J Med. 2025 Nov 13;393(19):1889-1900. doi: 10.1056/NEJMoa2504735
3. Eur Heart J. 2025 Nov 3;46(41):4156-4225. doi: 10.1093/eurheartj/ehaf191

Commentaries, Editorials, Guidelines, Reviews

4. Eur J Prev Cardiol. 2025 18:zwaf736. doi 10.1093/eurjpc/zwaf736
5. Stroke. 2025 Oct;56(10):3095-3098. doi: 10.1161/STROKEAHA.125.049900
6. JACC CardioOncol. 2025 Aug;7(5):578-579. doi: 10.1016/j.jaccao.2025.07.002
7. J Clin Invest. 2025 Jan 16;135(2):e185218. doi: 10.1172/JCI185218
8. Rev Esp Cardiol (Engl Ed). 2025 Mar;78(3):286-287. doi: 10.1016/j.rec.2024.11.013
9. Kardiol Pol. 2025;83(5):543-545. doi: 10.33963/v.phj.105682
10. Rev Esp Cardiol (Engl Ed). 2025 Jul;78(7):628-636. doi: 10.1016/j.rec.2024.11.009

RESEARCH GROUPS

Héctor Bueno
Multidisciplinary Translational Cardiovascular Research

Valentín Fuster
Cardiovascular Imaging and Population Studies

Pilar Martín
Regulatory Molecules of Inflammatory Processes

María Ángeles Moro
Neurovascular Pathophysiology

6 Cardiovascular Health Promotion

Coordinator: Rodrigo Fernández Jiménez
Clinical Leader: Valentín Fuster

Cardiovascular disease (CVD) remains one of the leading causes of death and disability worldwide, and its high prevalence and impact are largely driven by modifiable risk factors, such as smoking, unhealthy diet, and physical inactivity. Alarmingly, the burden is expected to increase due to rising rates of unhealthy lifestyles and obesity, particularly among children.

The Cardiovascular Health Promotion Program (CHPP) addresses this challenge through multidisciplinary studies and clinical trials conducted in collaboration with schools and communities. These initiatives target both children and adults, with the aim of implementing early prevention strategies and developing non-invasive technologies to support translational research and population studies on preclinical atherosclerosis.

The ultimate goal of the program is to reduce the personal and societal burden of CVD through health promotion and prevention strategies, with the potential to increase life expectancy and reduce the risk of other diseases, including dementia and cancer. The program focuses on three key objectives:

- Refining primordial prevention strategies in children and adolescents.
- Improving primary prevention by addressing the early, subclinical development and progression of atherosclerosis in young adults.
- Translating health-promotion initiatives to the general population.

The program comprises two research groups: Cardiovascular Imaging and Population Studies (PI, Valentin Fuster) and Cardiovascular Health and Imaging (PI, Rodrigo Fernández-Jiménez). In 2025, the program achieved significant scientific advances, summarized below.

Key Achievements in 2025

Gender-related differences in adolescents' cardiovascular health

Analysis from the SI! Program for Secondary Schools trial showed that overall cardiovascular health, measured using the American Heart Association's Life's Essential 8 score, declined during adolescence, with a greater decrease in boys than in girls (Figure 1) (1). Sex-related differences were observed in most individual cardiovascular health metrics, highlighting the need for sex-specific strategies to improve the effectiveness of adolescent health-promotion programs.

Impact of sleep on cardiac remodeling in adolescents

As part of the EnIGMA (Early ImaginG Markers of unhealthy lifestyles in Adolescents) project, sleep patterns were objectively assessed in 109 adolescents by accelerometry, combined with magnetic resonance imaging of the heart and liver. Shorter sleep duration was independently associated with adverse markers of cardiac remodeling and increased liver fat accumulation (2), emphasizing the importance of sleep health early in life and supporting its inclusion as a target for public health policy.

A community-based educational intervention for cardiovascular health and well-being

An interim two-year analysis of the Cardona Healthy Community 2030 program showed that participation in health-education workshops produced dose-dependent improvements in physical activity, adherence to the Mediterranean diet, and lipid and blood-pressure metrics *(JACC Advances, in press)*.

Beta-blocker therapy after myocardial infarction with preserved ejection fraction

Program researchers participated in the REBOOT trial, which showed that patients discharged after invasive care for myocardial infarction with left ventricular ejection fraction above 40% derived no benefit from long-term beta-blocker therapy, as measured as the incidence of death from any cause, reinfarction, or hospitalization for heart failure (5).

Cost-effectiveness of the cardiovascular polypill

An international multidisciplinary analysis of data from the SECURE trial demonstrated that the cardiovascular polypill is an effective and cost-effective strategy for secondary prevention, reducing cardiovascular events and healthcare costs in Spain *(Figure 2)* (3).

Inclusion of the cardiovascular polypill in the WHO List of Essential Medicines

A state-of-the-art review described the epidemiological need for, and barriers to, wider implementation of the cardiovascular polypill, a simple and scalable strategy for secondary prevention. The polypill is now included in several European guidelines for CVD management, and the World Health Organization has added it to the List of Essential Medicines, an important step toward expanding access to care worldwide, particularly in low- and middle-income countries *(Figure 3)* (4).

Funding, Outreach, and Recognition

Funding supporting studies involving program researchers included grants from the "la Caixa" Foundation (LCF/PR/CE16/10700001 and LCF/PR/MS19/12220001), Fundació la Marató de TV3 (369/C/2016), the ISCIII with European Union co-funding (PI19/01704 and PI22/01560), and the MSCA-COFUND Cure Heart & Brain program (GA 101126521).

The program also maintains strong outreach activity to promote cardiovascular health awareness. In 2025, members participated in public events, including the XXV Science and Innovation Week in Madrid.

Clinical leader Valentin Fuster received several distinctions, including the title of Doctor Honoris Causa from the European University of Cyprus, the Presidential Honorary Award from the President of Cyprus, and the Order of Merit of Duarte, Sánchez, and Mella from the Dominican Republic. He also delivered the inaugural World Heart Federation lecture at the European Society of Cardiology Congress 2025 in Madrid, where he received the WHF Lifetime Achievement Award.

Highlighted Publications

1. Eur J Prev Cardiol. 2025:zwaf210. doi: 10.1093/eurjpc/zwaf210
2. JACC Cardiovasc Imaging. 2025;18(9):1062-1064. doi: 10.1016/j.jcmg.2025.05.006
3. Lancet Reg Health Eur. 2025 Jun 27:55:101348. doi: 10.1016/j.lanepe.2025.101348
4. Nat Cardiovasc Res. 2025;4(3):259-265. doi: 10.1038/s44161-025-00619-z
5. N Engl J Med. 2025 Nov 13;393(19):1889-1900. doi: 10.1056/NEJMoa2504735

RESEARCH GROUPS

Rodrigo Fernández Jiménez
Cardiovascular Health and Imaging

Valentín Fuster
Cardiovascular Imaging and Population Studies

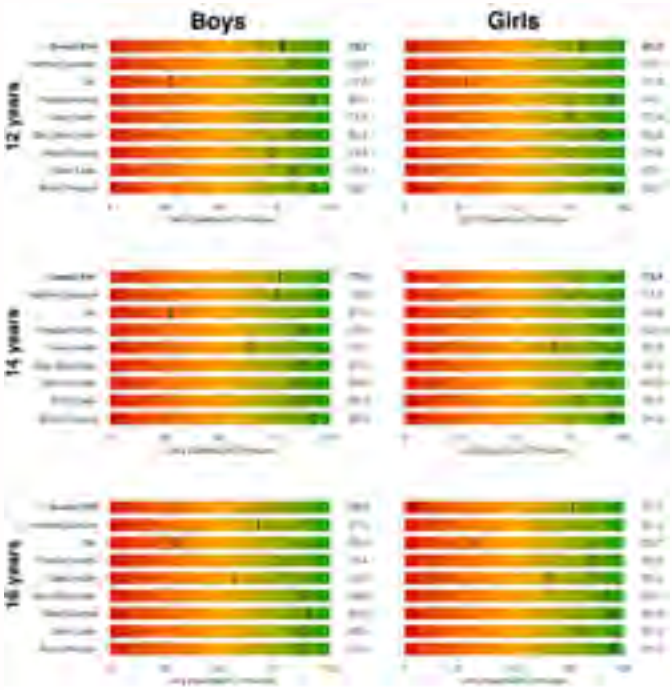


Fig1.
Scores for overall Life's Essential 8 (LE8) cardiovascular health (CVH) and each of the LE8 CVH metrics in boys and girls at 12, 14, and 16 years of age.
Study population size was 1324 (641 girls, 48.4%), 1211 (580 girls, 47.9%), and 1095 (528 girls, 48.2%) adolescents at 12, 14, and 16 years of age, respectively. The charts show mean scores (thick vertical black lines) and 95% confidence intervals (thin vertical lines). Reproduced from *Eur J Prev Cardiol*, 2025.

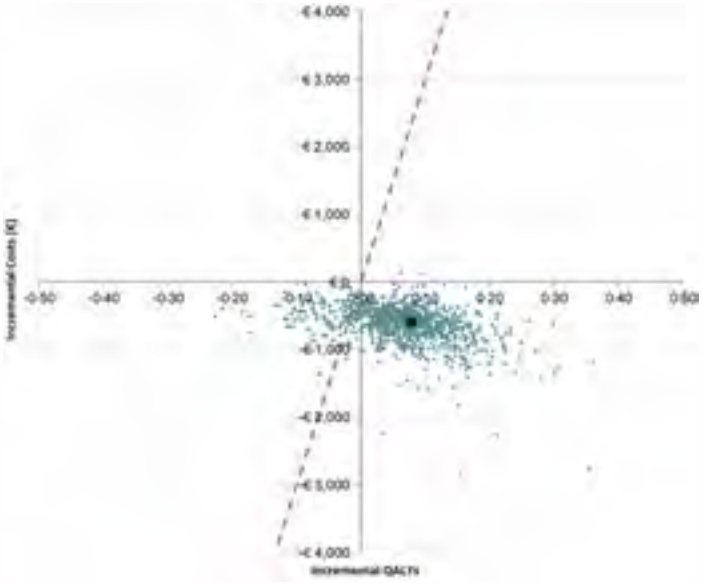


Fig2.
Cost-effectiveness analysis of the cardiovascular polypill for Spanish healthcare.
Cost-effectiveness plane from probabilistic sensitivity analysis. Most simulations fall in the southeast quadrant, below the €30,000 threshold per additional Quality-Adjusted Life Year (QALY) gained, indicating that the CV-Polypill is both less costly and more effective than standard care. Reproduced from Lancet Reg Health Eur, 2025

Fig3.
Road to the development and clinical impact of the cardiovascular polypill.
It has taken more than 20 years to move from conceptual debate to solid evidence supporting the cardiovascular polypill as a proven strategy for improving adherence and outcomes while serving as a cost-effective, affordable, and accessible intervention worldwide. 2023 marked a turning point, following inclusion of the polypill in several European CVD management guidelines. Its subsequent inclusion in the WHO's List of Essential Medicines represents a key step in global efforts to expand access to care and combat CVD. ESC, European Society of Cardiology; ESH, European Society of Hypertension. Reproduced from *Nat Cardiovasc Res*, 2025.

Back to Contents

7 Technology Development

Coordinator: Beatriz Álvarez

The eleven Technical Units (TUs) of the CNIC Technology Development Program (TDP) play a pivotal role in positioning the Center at the cutting edge of cardiovascular research. The TUs ensure that the CNIC remains a benchmark of scientific excellence through the development and implementation of advanced biomedical technologies, the provision of high quality internal and external services, and active engagement in training initiatives and collaborative funded projects

Our work is fully aligned with the CNIC's strategic vision, integrating state-of-the-art technological innovations, strengthening communication and protocol harmonization, and ensuring the highest quality standards. This commitment is underpinned by robust infrastructure support and ISOcertified quality management systems, with all Technical Units holding UNE-EN ISO 9001:2015 certification.

Key achievements in 2025

Deployment and optimization of the equipment acquired under the previous EQC2024 call, funded by the Ministry of Science, Innovation, and Universities, ensuring its readiness and maximal scientific impact:

1. Through EQC2024-007986-P, the Clinical Trials Coordination Unit (CTCU) acquired a spectral CT scanner at the end of 2024, and this equipment is now available to researchers.
2. Thanks to EQC2024-008058-P, the Metabolomics platform finalized the tender to acquire a high-sensitivity mass spectrometer for targeted lipidomics and metabolomics.
3. Through EQC2024-008109-P, the Advanced Imaging Unit purchased two ultrasound systems, now available to researchers for work with small animal models.
4. The Microscopy Unit incorporated a multimodal spinning-disk, high-resolution epifluorescence microscope with real-time image restoration and on-the-fly deconvolution. Thanks to the EQC2024-008059-P the system, the first of its kind in Spain, produces images with confocal-level quality.
5. Through EQC2024-008195-P, the Bioinformatics unit acquired and deployed equipment to build a computational platform for storing and analyzing biomedical images. The platform includes 16 new NVIDIA H100 cards to support the use of AI algorithms in CNIC projects. This project also includes renewal of the CNIC CPD cooling system.

The TUs play a key role in the CNIC's scientific activity by providing specialized expertise, methodological support, and technological implementation, enabling high-quality data generation and strengthening research competitiveness. Their close collaboration with researchers also promotes service innovation and enhances scientific capacity.

In 2025, this joint effort resulted in 88 publications, 78% of them research articles. Of these, 85% (75 documents) were published in Q1 journals and 58% (51 documents) in D1 journals, and 65% (57 documents) involved international collaboration. The TUs also contributed to four Highly Cited Papers (HCPs), ranking in the top 1% most cited publications in their subject category over the past decade.

Training is a core pillar of the CNIC, and the TDP supports this mission through participation in the UAM Master's Program in Molecular Biomedicine and in initiatives such as Acércate, Res@cnic, the CNIC Seminar Series, Science Week, and Researchers' Day.

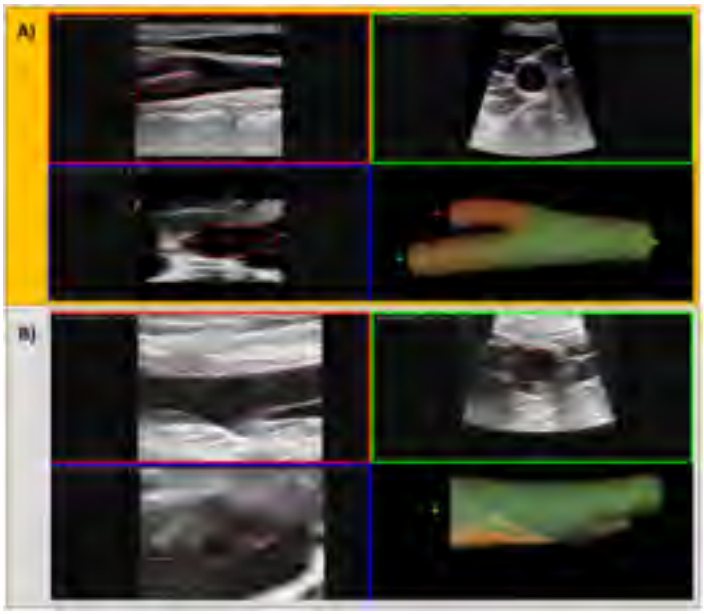


Fig1.
3D imaging and reconstruction of atherosclerotic plaque in the carotid artery. Images in (A) show a carotid artery free of plaque, while images in B) show a carotid artery with atherosclerotic plaque.

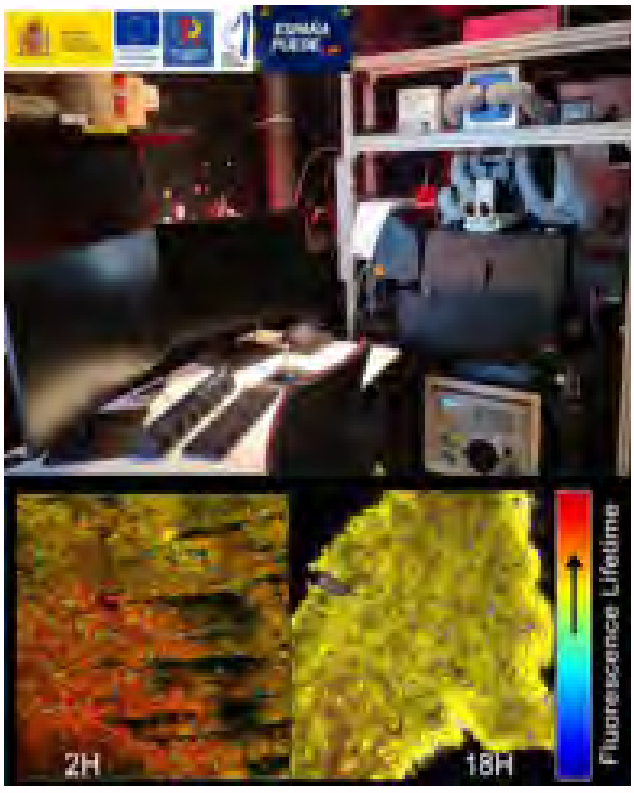


Fig2.
FLIM imaging of doxorubicin in heart. The FLIM platform (top) can monitor the intracardiac clearance of doxorubicin and its cardiotoxic metabolite in freshly excised mouse heart tissue (bottom). Using intrinsic fluorescence-lifetime contrast, the drug distribution was assessed at 2, 12 and 24 and hours after in-vivo administration. The longer fluorescence lifetimes (red areas) detected at 2 hours indicate substantial drug accumulation within cardiac tissue, which persists predominantly as metabolic derivatives localized mainly in cardiomyocyte nuclei at 12 hours [FLIM images were generated in collaboration with Laura Cádiz and Borja Ibáñez from the Translational Laboratory for Cardiovascular Imaging and Therapy].

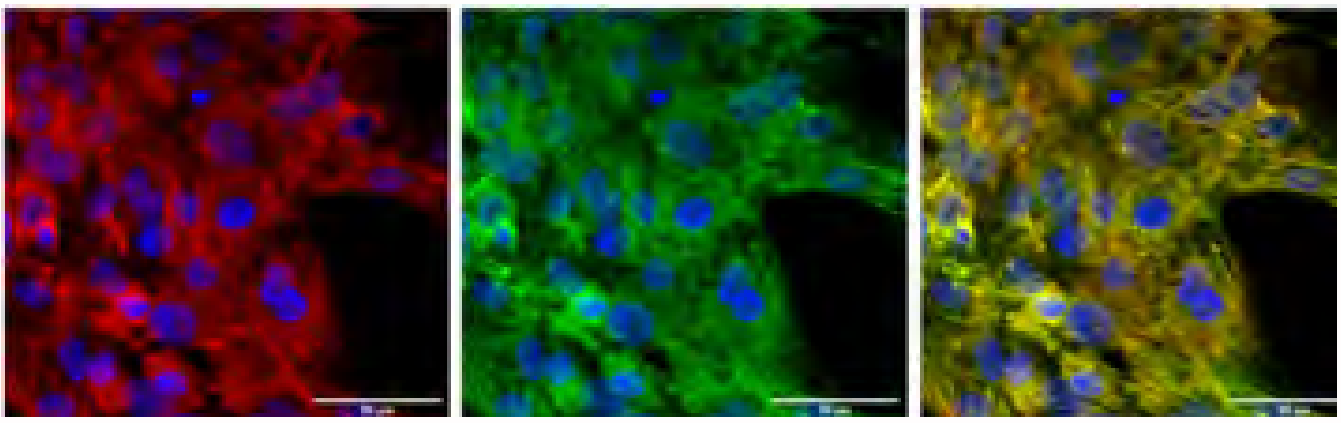


Fig3.
CRISPR-Cas9 strategy for generating compound heterozygous human induced pluripotent stem cell–derived cardiomyocytes (hiPSC-CMs). The hiPSC-CM line contains eGFP and HaloTag reporters knocked into the same genomic position on each titin (TTN) allele. [hiPSC-CMs were generated by the Pluripotent Cell Technology Unit.]

TECHNICAL UNITS

Fátima Sánchez Cabo
Bioinformatics

Antonio J. Quesada
Clinical Trial Coordination
Advanced Imaging (Acting Head)

Beatriz Álvarez
Flow Citometry

Comparative Medicine

Ana Dopazo
Genomics

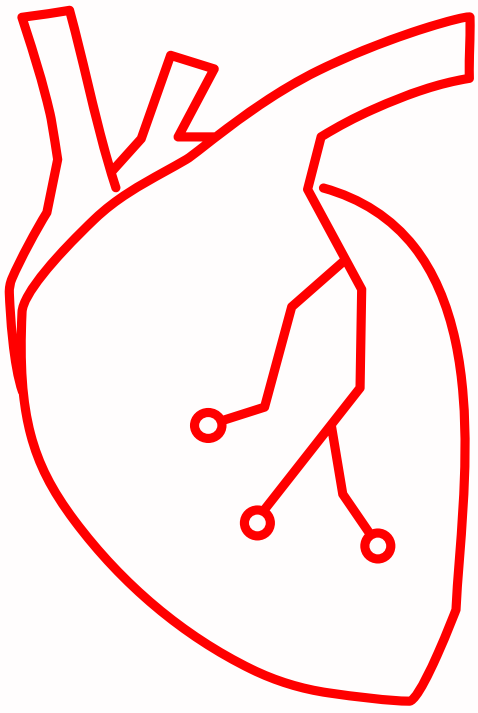
Valeria Caiolfa
Microscopy

Giovanna Giovinazzo
Pluripotent Cell Technology

Juan Antonio López
Proteomics

Juan De Dios Hourcade
Transgenesis

Juan A. Bernal
Viral Vectors



Clinical Studies at the CNIC

Translational research plays a vital role in turning laboratory discoveries into real-world medical solutions. By bridging the gap between science and practice, this research helps develop new treatments, diagnostic tools, and prevention strategies that directly benefit patients. This approach combines insights from basic science with clinical expertise to accelerate medical progress and improve healthcare outcomes.

This patient-oriented approach is a cornerstone of our work at the CNIC. We are committed to advancing these studies and ensuring their impact on patient care through the clinical guides. Below, we highlight the clinical projects that were active in 2025.

PESA-Health-CNIC-Santander: Early Detection of Subclinical Atherosclerosis, Disease Progression, and Cardiovascular Health

Principal Investigator: **Valentín Fuster**

PESA Health Initiative

The PESA-Health-CNIC-Santander Study builds on the original PESA Study, launched in 2010 by the CNIC in collaboration with Santander Bank. That study enrolled 4,184 asymptomatic individuals aged 40–55 to detect subclinical atherosclerosis (SA) long before symptoms arise and to investigate the factors driving its development and progression.

PESA-Health extends this work by following the same participants for an additional 10 years. The expanded program incorporates new research areas, including the links between SA and Alzheimer's disease or cognitive decline, the role of age-related somatic mutations, and how these mutations may influence cardiovascular events and SA progression.

As in the original PESA Study, PESA-Health employs advanced imaging technologies, including 3D vascular ultrasound of the carotid arteries and aorta, coronary artery calcium quantification by computed tomography, cardiac magnetic resonance imaging, coronary CT angiography (CTA), PET, and PET-amyloid analysis. The protocol also includes extensive biosampling for multi-omics analysis, alongside new substudies examining the association between SA and sleep apnea.

As the CNIC's flagship study, PESA-Health brings together numerous clinical and basic research groups across the center. Findings from the original PESA Study have already contributed substantially to our understanding of the origins and progression of atherosclerosis.

PESA-Health began in February 2020, with 3,496 original PESA participants continuing in the new phase. By the end of 2025, 319 participants had completed the second round of follow-up visits, corresponding to the fifth visit since the PESA Study's inception in 2010.

REACT: Reversal of Early Atherosclerosis through Personalized Curative Treatment

Principal Investigator: **Borja Ibáñez**

Atherosclerosis—the progressive accumulation of plaque within arterial walls—is the leading cause of cardiovascular disease worldwide. As cholesterol, lipids, inflammatory cells, and other components build up over time, arteries narrow and blood flow to vital organs is reduced. The process often begins early in life, progresses silently, and can affect multiple vascular territories, contributing substantially to global morbidity and mortality.

To address this major health challenge, the CNIC and Rigshospitalet in Copenhagen have launched Phase 1 of the REACT project (Reversal of Early Atherosclerosis through Personalized Curative Treatment), funded by the Novo Nordisk Foundation. The primary goal of this phase is to determine the prevalence of asymptomatic (silent) atherosclerosis in a European-ancestry cohort across a broad age range (18–70 years). This will be achieved through advanced imaging techniques and circulating biomarkers, integrated with conventional cardiovascular risk factors.

Phase 1 is a large-scale prevalence study involving 16,000 participants (8,000 in Spain and 8,000 in Denmark). The study combines vascular ultrasound (3DVUS), coronary artery calcium scoring, CT angiography (CTA), and biomarker analysis to generate a detailed age-stratified profile of subclinical atherosclerosis. The findings will support the development of a more precise risk stratification algorithm than those currently in use.

The Phase 1 results will inform the design of Phase 2, a randomized clinical trial evaluating whether early, imaging-guided intervention—including lifestyle modification, non-pharmacological strategies, and lipid-lowering therapy—can reduce atherosclerotic plaque burden or even promote regression.

By the end of 2025, 5,714 participants aged 18–70 years (2,825 women and 2,889 men) had been enrolled. Recruitment is expected to reach the target of 8,000 participants by June 2026.

RESILIENCE: Remote Ischemic CondItioning in Lymphoma Patients Receiving Anthracyclines

Principal Investigator: **Borja Ibáñez**

H2020 Grant No. 945118

Anthracyclines are a widely used class of anticancer drugs, administered to more than 3 million of the approximately 4 million patients diagnosed with cancer each year in Europe. Although highly effective, these drugs carry a substantial risk of cardiotoxicity: recent data indicate that more than 35% of treated patients develop some degree of cardiomyopathy. This trade-off between cancer control and long-term heart failure (HF) represents a growing clinical and healthcare challenge, with significant consequences for cancer survivors.

Remote ischemic preconditioning (RIPC) offers a potential strategy to mitigate this risk. RIPC is a non-invasive, safe, and cost-effective procedure involving brief, reversible episodes of ischemia—typically induced in a limb—followed by reperfusion. These cycles activate systemic protective mechanisms that can reduce tissue injury during subsequent ischemic events. Experimental studies in large-animal models have shown that 3–5 cycles of 5-minute limb ischemia followed by 5-minute reperfusion reduce infarct size after induced myocardial ischemia. Importantly, evidence suggests that RIPC must be applied before the damaging event to confer protection. Because chemotherapy is a planned intervention, anthracycline-induced cardiomyopathy provides a well-defined setting in which to test this approach.

RESILIENCE is a multinational, phase II, double-blind, sham-controlled, randomized clinical trial evaluating the efficacy and safety of RIPC in patients with lymphoma or breast cancer who are receiving treatment with anthracyclines. Eligible patients scheduled to receive ≥240 mg/m^2 of anthracyclines undergo baseline cardiac magnetic resonance (CMR) imaging and blood testing for high-sensitivity troponin (hsTn) and NT-proBNP. Patients with a CMR-confirmed left ventricular ejection fraction >40% are randomized 1:1 to receive either RIPC or a sham procedure.

Nine weeks after completing chemotherapy, participants undergo repeat CMR imaging and biomarker assessment. Clinical follow-up visits are scheduled at 12, 18, 30, and 42 months, continuing until the final CMR evaluation is completed.

The trial aims to enroll 608 patients across 22 sites in six European countries (Spain, Portugal, France, Germany, the Netherlands, and Denmark). Funded by the European Commission (Grant Agreement No. 945118-RESILIENCE), RESILIENCE began its grant period in June 2021, with patient recruitment starting in 2022. Recruitment is expected to conclude in December 2026. By the end of 2025, all 22 sites remained active, and 445 participants had been enrolled.

REBOOT: Treatment with Beta-blockers after Myocardial Infarction Without Reduced Ejection FracTion

Principal Investigator: **Borja Ibáñez**

The routine use of beta-blockers for patients after myocardial infarction (MI) is largely supported by clinical trials conducted before the widespread adoption of reperfusion strategies. Although these agents provide clear benefit in patients with reduced left ventricular ejection fraction, their value in patients with preserved ejection fraction has remained unclear. Despite this limited evidence, more than 80% of post-MI patients in this category are prescribed lifelong beta-blocker therapy.

The REBOOT trial was designed to address this gap by evaluating whether beta-blocker therapy improves outcomes in post-MI patients with a left ventricular ejection fraction greater than 40%. This multinational, randomized study enrolled 8,506 patients, who were assigned either to receive beta-blockers (with the specific agent and dose determined by the treating physician) or to receive no beta-blocker therapy. The primary endpoint was a composite of all-cause mortality, reinfarction, or hospitalization for heart failure over a median follow-up of 3 years.

Coordinated by the CNIC Clinical Trials Coordination Unit and conducted in collaboration with the Mario Negri Institute of Pharmacological Research in Milan, the trial involved 77 hospitals in Spain and 29 in Italy.

In total, 4,243 patients were assigned to beta-blocker therapy and 4,262 to no beta-blocker therapy; after exclusions, 8,438 patients were included in the main analysis. Among patients discharged after invasive management of myocardial infarction with preserved ejection fraction (>40%), beta-blocker therapy did not reduce the incidence of death from any cause, reinfarction, or hospitalization for heart failure.

In 2025, the results were published in three papers, two in The New England Journal of Medicine (doi: 10.1056/NEJMoa2504735); (doi: 10.1056/NEJMoa2512686) and one in The Lancet. (doi: 10.1016/S0140-6736(25)01592-2). Full details are presented in the Scientific Highlights section.

MRVALVE: Multimodality Myocardial Tissue Characterization in Patients with Significant Valvular Disease

Principal Investigator: **Borja Ibáñez**

The MRVALVE study uses a multimodality imaging strategy—combining cardiac magnetic resonance (CMR) and strain echocardiography—to characterize left ventricular (LV) structure, function, and tissue composition in patients with significant valvular heart disease (VHD). The study focuses on the two most common forms of VHD: aortic stenosis (AS) as a model of chronic LV pressure overload, and mitral regurgitation (MR) as a model of LV volume overload.

Valvular heart disease profoundly affects LV dimensions, function, and myocardial tissue properties, all of which are central to clinical decision-making. Current guidelines recommend surgical or percutaneous intervention once symptoms develop or when there is clear evidence of LV remodeling or dysfunction. However, disease progression—from asymptomatic stages to overt symptoms, and from preserved function to dilatation, hypertrophy, and failure—is driven by underlying myocardial changes, including cardiomyocyte loss, extracellular matrix expansion, and fibrosis.

Although valve repair or replacement is effective in severe VHD, intervention is typically triggered by symptoms or measurable LV dysfunction. By that stage, myocardial damage may already be partially reversible. MRVALVE addresses the need for earlier detection of myocardial involvement in asymptomatic patients, enabling better timing of intervention before permanent structural damage occurs.

CMR serves as the reference standard for anatomical and functional cardiac assessment. The procedure detects focal fibrosis using late gadolinium enhancement and enables advanced tissue characterization through parametric T1/T2 mapping, calculation of extracellular volume (ECV, a marker of diffuse fibrosis), and absolute myocardial perfusion assessment. These techniques require gadolinium-based contrast agents, which have an established safety profile. Hematocrit measurement is incorporated to refine ECV calculation.

Strain echocardiography provides sensitive assessment of myocardial deformation and can detect multidirectional strain abnormalities even when global LV function appears preserved. In MRVALVE, imaging findings are correlated with functional capacity measured by the six-minute walk test. Cardiac computed tomography is also performed to quantify coronary and valvular calcium deposition, generating a calcium score with diagnostic and prognostic relevance, particularly in AS.

To date, 71 patients have been enrolled, and all have completed their 1-year follow-up visit.

MATRIX: Novel Mitochondria-targeted Therapies for Cancer Treatment–induced Cardiotoxicity

Principal Investigator: **Borja Ibáñez**
ERC Consolidator Grant No. 819775

The MATRIX Project aims to develop innovative therapies for cancer treatment–induced cardiotoxicity (CTiCT), a major limitation of modern oncology. This initiative is a joint effort between the CNIC and Fundación Jiménez Díaz University Hospital, building on a collaborative program established in 2015 to study myocardial diseases.

Although advances in cancer therapy have improved survival among the approximately 4 million patients diagnosed annually in Europe, many treatments carry significant cardiovascular risk. CTiCT affects up to 25% of patients receiving anthracyclines or trastuzumab and can lead to progressive cardiomyopathy, chronic heart failure, or death. This adverse effect represents a serious long-term burden for cancer survivors.

Current strategies for managing CTiCT remain suboptimal. Early detection tools lack sensitivity, and available heart failure therapies are largely nonspecific. Recent findings from our group suggest that CTiCT is closely associated with altered mitochondrial dynamics and subsequent metabolic reprogramming in cardiomyocytes.

MATRIX addresses this challenge through a comprehensive, mitochondria-centered approach. We hypothesize that early-stage CTiCT may be reversible through targeted metabolic reprogramming aimed at restoring mitochondrial substrate utilization. To enable timely intervention, the project incorporates a novel imaging-based algorithm developed by our team to detect subclinical myocardial injury in patients receiving commonly used anticancer drugs before conventional clinical parameters become abnormal.

In advanced stages of CTiCT, where mitochondrial dysfunction may be irreversible, MATRIX explores a more radical strategy: in vivo mitochondrial transplantation to replenish damaged myocardium with functional mitochondria.

The project has strong translational potential, spanning early diagnostic technologies, novel therapeutic strategies, and mechanistic insights into the pathophysiology of CTiCT.

Patient recruitment began in 2020. By the end of the study, 56 participants were enrolled, and the first results have been submitted for publication.

PRECOGNITIVE: Effect of Remote Ischemic Preconditioning on Cognitive Function and Cerebral Vasculature

Principal Investigator: **Gonzalo Pizarro Sánchez**

Arterial hypertension can damage the cerebral vasculature even when blood pressure is adequately controlled. Current therapies primarily focus on managing blood pressure and preventing target-organ injury, including damage to the brain. Remote ischemic preconditioning (RIPC), first shown more than 30 years ago to protect organs such as the heart and brain in experimental models, has since been translated into clinical research. The technique consists of repeated cycles of cuff inflation and deflation on the arm—typically 4 cycles of 5 minutes each. The brief, controlled ischemia induced in the limb activates systemic protective mechanisms that may shield distant organs, including the brain, from subsequent ischemic injury.

Our research has contributed substantially to this field, with recent studies demonstrating that RIPC can improve cognitive performance and cerebral vascular function in patients with vascular dementia. PRECOGNITIVE is a proof-of-concept randomized clinical trial involving 45 women with hypertension and evidence of target-organ damage, such as left ventricular hypertrophy. Participants are allocated to one of three groups:

1.- **RIPC group:** undergoes the RIPC procedure, with the cuff inflated to 20 mmHg above systolic blood pressure.
2.- **RIPC-sham group:** follows the same protocol, but the cuff is inflated only to 50 mmHg, insufficient to induce ischemia.
3.- **Control group:** receives no cuff intervention.

The study evaluates whether RIPC exerts a protective effect on the cerebral vasculature in hypertensive patients without significant cognitive impairment. Outcomes are assessed using comprehensive neurocognitive testing and non-invasive imaging, including echocardiography, non-contrast brain magnetic resonance imaging, and transcranial Doppler ultrasound.

As of the end of 2025, 15 patients had been recruited.

MACADAMIA: Characterization of Cardiac Metabolism Using Multimodal Imaging in Idiopathic Cardiomyopathy

Principal Investigator: **Borja Ibáñez**

Heart failure (HF) remains one of the most significant health challenges in modern societies, placing a heavy burden on healthcare systems. Developing effective therapies requires a deeper understanding of the mechanisms that drive the onset and progression of HF.

The heart is the most energy-demanding organ relative to its size. Under physiological conditions, it derives most of its ATP from fatty acid β-oxidation (approximately 60%), with carbohydrate metabolism via the Krebs cycle providing most of the remaining energy. Other substrates, such as amino acids, contribute minimally to overall energy production.

In HF, however, the myocardium undergoes a metabolic reprogramming often referred to as the "metabolic switch," characterized by a shift from fatty acid oxidation toward a greater reliance on glucose metabolism. Although initially considered an adaptive response, accumulating evidence from experimental and clinical studies suggests that this shift may be energetically inefficient and contribute to progressive contractile dysfunction.

Our group has shown that the metabolic switch plays a central role in heart failure secondary to idiopathic dilated cardiomyopathy (IDCM). In mouse models, a diet rich in fatty acids reversed metabolic remodeling and improved cardiac phenotype. Similar findings were observed in pigs, whose metabolism more closely resembles that of humans.

Before initiating an interventional clinical trial in IDCM, it is essential to determine how prevalent the metabolic switch is in patients. The MACADAMIA study addresses this question through an observational analysis of a cohort of patients with IDCM. Using multimodal imaging—including transthoracic echocardiography with strain analysis, cardiac magnetic resonance (CMR), and positron emission tomography/computed tomography (PET/CT) with the radiotracer 18F-FDG—the study characterizes myocardial metabolic profiles without therapeutic intervention.

As of February 2026, 43 patients had been enrolled.

In the medium to long term, a randomized clinical trial is planned in IDCM patients demonstrating evidence of the metabolic switch. Participants will be assigned either to a fatty acid–enriched dietary intervention or to a standard diet, with outcomes assessed by CMR (cardiac function) and PET/CT (metabolic activity).

ATTRACKING CNIC: The ATTRACKING Registry

Principal Investigator: **Pablo García-Pavía**

Tafamidis, acoramidis and vutrisiran are approved therapies for transthyretin amyloid cardiomyopathy (ATTR-CM), a rare and life-threatening disease caused by the buildup of transthyretin amyloid fibrils in the heart. The pivotal clinical trials demonstrated that these medications reduce mortality and cardiovascular hospitalizations. However, as with many pivotal trials, the study population may not fully reflect contemporary clinical practice.

Recent advances in diagnostic imaging and disease awareness have enabled earlier detection of ATTR-CM, resulting in changes in patient profiles and overall prognosis compared with those enrolled in the original trial.These shifts raise important questions about the effectiveness and safety of tafamidis in routine care.The ATTRACKING CNIC registry was established to evaluate ATTR-CM medications in a real-world, unselected cohort of patients with ATTR-CM across Spain.

Objectives

1. To characterize the contemporary Spanish population of patients with ATTR-CM treated with ATTR-CM medications.
2. To assess the safety profile of ATTR-CM medications in routine clinical practice.
3. To compare real-world outcomes with those reported in the privotal trials.

Study Design

ATTRACKING CNIC is a prospective, multicenter, non-randomized observational registry enrolling patients diagnosed with ATTR-CM who initiate treatment with ATTR-CM medications.

As of February 2026, agreements have been signed with 51 hospitals, and 521 participants have been enrolled.

TAILOR-AF: Patient-specific Ablation of Persistent Atrial Fibrillation Drivers Guided by Frequency and Amplitude Modulation Criteria

Principal Investigator: **David Filgueiras**

Co-Promoters: CNIC and Hospital Universitario Clínico San Carlos

Pulmonary vein isolation (PVI) is the cornerstone of catheter ablation for persistent atrial fibrillation (AF). However, despite more than two decades of clinical use, long-term success rates remain modest. Approximately 40% of patients remain free of AF at 12 months following ablation without antiarrhythmic drug therapy, underscoring the need for more individualized treatment strategies.

To address this limitation, our group has developed a computational mapping tool that enables interventional electrophysiologists to identify atrial "driver regions" responsible for maintaining persistent AF. Using conventional electroanatomic mapping systems and multielectrode catheters, these regions are localized through novel signal-processing algorithms that analyze frequency and amplitude modulation of atrial electrograms during fibrillation. The algorithms—publicly available (Quintanilla JG et al. Circ Res. 2019;125:609–627)—quantify individual frequency modulation (iFM) and amplitude modulation (iAM), allowing precise identification of rotational activity and leading AF drivers.

The primary goal of the TAILOR-AF study is to apply iAM/iFM-guided mapping to identify and ablate the dominant drivers in patients with symptomatic persistent AF despite having undergone two or more prior PVI procedures. Secondary objectives include the evaluation of circulating biomarkers, advanced atrial imaging parameters, and surface electrocardiographic phenotypes associated with atrial remodeling. In selected patients undergoing minimally invasive thoracoscopic ablation, left atrial appendage tissue samples are collected to investigate the molecular mechanisms underlying AF maintenance.

As of the end of 2025, recruitment had been completed, and 80% of participants had finished the 1-year follow-up to assess arrhythmia recurrence. The results are expected to be communicated to the scientific community and the broader public during the third quarter of 2026.

SIR-CVT: Spanish Immunotherapy Registry – Cardiovascular Toxicity

Co-Promotors: Sociedad Española de Cardiología, Sociedad Española de Oncología Médica

SIR-CVT is a prospective, non-interventional registry with two primary objectives:

1. To evaluate risk factors and current clinical management practices related to cardiovascular (CV) toxicity in patients with solid tumors receiving immune checkpoint inhibitors (ICIs) for approved indications.
2. To validate the human homolog of miR-721 as a biomarker for the early diagnosis of immunotherapy-induced myocarditis.

In addition, the study addresses several secondary objectives:

- To identify clinical, electrocardiographic, imaging, laboratory, and genetic markers associated with early diagnosis of ICI-related myocarditis.
- To detect markers of other ICI-related CV toxicities beyond myocarditis.
- To evaluate the association between prior chemotherapy exposure and subsequent ICI-related CV risk.
- To investigate the pathogenic mechanisms underlying myocarditis induced by immune checkpoint blockade (anti–PD-L1/PD1 and anti–CTLA4 therapies).
- To assess the impact of structured CV monitoring on patients' quality of life and perceived quality of care.

After a baseline visit, participants are managed according to standard clinical practice, including routine follow-up schedules determined by their treating physicians. Patients are followed for 12 months after enrollment, or until death or loss to follow-up. All data collected are used exclusively for research purposes.

As of February 2026, 10 patients had been enrolled and had undergone cardiac magnetic resonance imaging and echocardiographic evaluation at the CNIC.

HF4HF: Cardiac Metabolic Reprogramming by Nutritional Intervention — High-Fat Diet for Heart Failure

Principal Investigator: **Borja Ibáñez**
Co-PI: **Pablo García-Pavía**

The heart is a highly energy-dependent organ that requires a continuous supply of ATP to sustain contractile function. Cardiac mitochondria generate this energy using multiple substrates, including fatty acids, glucose, and, to a lesser extent, amino acids. Under physiological conditions, fatty acid β-oxidation provides the majority of myocardial ATP, as it is the most energy-dense substrate.

In heart failure (HF), however, the myocardium undergoes metabolic reprogramming characterized by a shift from fatty acid oxidation toward increased reliance on glucose metabolism. Although initially considered adaptive, growing evidence suggests that this "metabolic switch" may contribute to impaired energetic efficiency and progressive contractile dysfunction.

HF4HF is funded by the ERA4Health Partnership and is coordinated by the CNIC. Participating institutions include the Fundación para la Investigación Biomédica Hospital Universitario Puerta de Hierro (IIS Majadahonda, Spain), INSERM (France), the University of Medicine and Pharmacy "Carol Davila" (Bucharest, Romania), and the University of Florence (Italy).

This project brings together a multidisciplinary consortium including cardiologists, nutrition specialists, imaging experts, and industry partners focused on heart failure.

Our consortium has demonstrated in experimental models that a high-fat dietary intervention can reverse this metabolic shift, restoring fatty acid utilization in cardiac mitochondria and improving cardiac function. These findings provide the mechanistic basis for translating this concept into a clinical setting.

HF4HF is a pilot clinical study designed to evaluate whether a structured high-fat dietary program can favorably modulate cardiac metabolism in patients with HF. The intervention will be assessed using state-of-the-art non-invasive imaging techniques to quantify changes in cardiac function and metabolic substrate utilization. Complementary translational analyses will be performed in explanted human hearts and in blood samples from experimental models and enrolled patients. Additional preclinical studies will examine whether different fat-based dietary compositions exert metabolic effects on the failing myocardium.

At the end of 2025, a substantial protocol amendment aimed at facilitating recruitment through revised eligibility criteria was approved by the Hospital Puerta de Hierro ethics committee (December 19, 2025). The amendment is currently being prepared for submission in Italy, France, and Romania. To strengthen recruitment, Fundación Jiménez Díaz University Hospital has joined the study as an additional center, with local ethics approval already obtained. As of February 2026, two participants had been enrolled. Recruitment is expected to accelerate once the remaining regulatory approvals are secured.

DIREQT2Heart: Direct quantitative assessment of myocardial perfusion using cardiovascular magnetic resonance imaging

Principal Investigators: **Borja Ibáñez (CNIC), Javier Escaned (Hospital Universitario Clínico San Carlos)**

Coronary artery disease—whether involving epicardial vessels or the microvasculature—is the leading cause of myocardial ischemia due to impaired coronary perfusion. The current reference standard for assessing coronary flow is invasive cardiac catheterization with physiological measurements, such as coronary thermodilution. Although highly accurate, these procedures carry procedural risks.

Several non-invasive imaging techniques have been developed to estimate myocardial perfusion, including SPECT-MIBI and computed tomography. However, most available methods provide qualitative or semi-quantitative information, limiting their diagnostic accuracy in complex scenarios such as three-vessel disease or microvascular dysfunction.

Cardiovascular magnetic resonance (CMR) is the reference modality for evaluating cardiac structure and function. In recent years, quantitative perfusion sequences have been introduced, enabling measurement of absolute myocardial blood flow. Nonetheless, these sequences remain constrained by limited spatial resolution and incomplete cardiac coverage.

To overcome these limitations, our group has developed a novel CMR sequence—DIREQT—that enables highly accelerated image acquisition, improving temporal resolution and myocardial coverage while generating fully quantitative perfusion maps. This approach has the potential to provide a more precise and comprehensive assessment of myocardial blood flow.

The objective of DIREQT2Heart is to validate the DIREQT sequence against the invasive reference standard of coronary thermodilution. The study aims to enroll 30 patients representative of the clinical populations in which this technique would be applied. Participants are divided into three groups:

1. Patients with significant epicardial disease of the proximal-to-mid left anterior descending artery.
2. Patients with microvascular disease (structural endotype).
3. Control patients without significant epicardial disease and with preserved coronary flow reserve.

Patients undergoing clinically indicated coronary angiography and physiological assessment at Hospital Clínico San Carlos are invited to participate. Those who provide informed consent are referred to the CNIC for CMR evaluation using the DIREQT sequence.

As of February 2026, 10 patients had been enrolled and had completed the CMR examination.

PATAGONIA: Prevalence of Vascular Toxicity Among long-term Cancer SurvivorsTreated with Anthracyclines

Principal Investigator: **Inés García-Lunar**
Promotor: Centro Nacional de Investigaciones Cardiovasculares (CNIC)
Participating centers: CNIC; Unidad de Oncohematología Pediátrica, Hospital La Paz; Servicio de Hematología, Fundación Jiménez Díaz; Servicio de Cardiología, Hospital Universitario Puerta de Hierro.

Cardiovascular disease (CVD) and cancer are the two leading causes of mortality worldwide and are increasingly interconnected. Anthracyclines (ACs) are widely used chemotherapeutic agents for both hematologic malignancies and solid tumors. Although highly effective, ACs are associated with cardiotoxicity, which may manifest years after treatment and often progresses to heart failure. As cancer survival has improved substantially over recent decades, the burden of CVD among long-term survivors has also risen, representing a growing public health challenge.

The mechanisms underlying AC-related cardiotoxicity remain incompletely understood, and no targeted preventive therapies have yet demonstrated clear efficacy. Most research has focused on direct myocardial injury. However, accumulating experimental and early clinical evidence suggests that AC-induced vascular damage may precede overt cardiac dysfunction. We hypothesize that AC-related vascular injury may remain subclinical for years and contribute to the later development of heart failure.

PATAGONIA addresses this hypothesis through a comprehensive evaluation of vascular function in long-term cancer survivors previously exposed to ACs. Using state-of-the-art, non-invasive, radiation-free imaging techniques at the CNIC, the study assesses both coronary and peripheral vascular function. Findings are compared with those from non-exposed control participants.

The distinctive feature of PATAGONIA, compared with other contemporary survivor cohorts, is its primary focus on vascular dysfunction as a potential mechanistic driver of subsequent cardiac disease. By identifying early vascular abnormalities, the project aims to develop new strategies for risk stratification and early detection of AC-related cardiovascular damage.

As of February 2026, 50 patients had been enrolled and had undergone cardiac magnetic resonance imaging and vascular ultrasound assessment at the CNIC.

3 Scientific Highlights

BY PUBLICATION DATE

Back to Contents

Immunity

CNIC SCIENTISTS DISCOVER HOW THE GUT MODULATES THE DEVELOPMENT OF INFLAMMATORY CONDITIONS

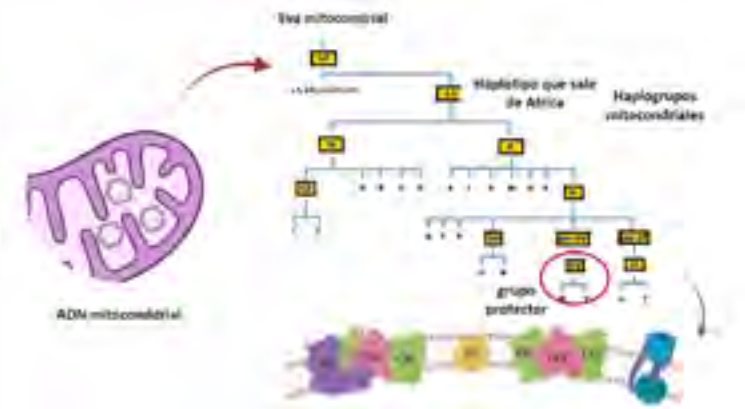
This study, led by Dr. David Sancho, reveals how increased intestinal permeability allows natural gut bacteria to cross the intestinal barrier and reach the bone marrow, where they induce epigenetic changes—modifications that alter gene activity without affecting DNA sequence—in the stem cells that give rise to immune cells. The epigenetic changes induced by the translocated gut bacteria generate "trained" immune cells that are primed to respond more efficiently to future infections. However, this same ability to amplify the immune response can also aggravate inflammatory conditions such as cardiovascular and neurodegenerative diseases. The new study highlights the key role in this process of a protein called Mincle, expressed in cells of the innate immune system.

The study was funded by the Spanish Ministerio de Ciencia, Innovación y Universidades-Agencia Estatal de Investigación (AEI); the European Union NextGenerationEU/PRTR; the Comunidad de Madrid; Fundación Científica de la Asociación Española Contra el Cáncer; Worldwide Cancer Research; the European Research Council; Inmunotek S.L.; and Fundación "la Caixa".

- Robles-Vera I, Jarit-Cabanillas A, Brandi P, Martínez-López M, Martínez-Cano S, Rodrigo-Tapias M, Femenía-Muiña M, Redondo-Urzainqui A, Nuñez V, González-Correa C, Moleón J, Duarte J, Conejero L, Mata-Martínez P, María Díez-Rivero C, Bergón-Gutiérrez M, Fernández-López I, Gómez MJ, Quintas A, Dopazo A, Sánchez-Cabo F, Pariente E, Del Fresno C, Subiza JL, Iborra S, Sancho D. Microbiota translocation following intestinal barrier disruption promotes Mincle-mediated training of myeloid progenitors in the bone marrow. Immunity 2025 Feb 11;58(2):381-396.e9. doi: 10.1016/j.immuni.2024.12.012. Epub 2025 Jan 22. PMID: 39848243 PMCID: PMC11832192

Communications Biology

THE EUROPEAN MITOCHONDRIAL LINEAGE MAY PROTECT AGAINST SEVERE FORMS OF COVID-19



This study showed that specific genetic variants in the mitochondrial DNA of Europeans may protect them against the more severe forms of COVID-19. The results of the study provide new clues to the origin of individual differences in the response to infection. The research was led by Dr. José Antonio Enríquez, head of the GENOXPHOS group at the CNIC and a member of the Spanish research network on frailty and healthy aging (CIBERFES).

- Cabrera-Alarcon JL, Cruz R, Rosa-Moreno M, Latorre-Pellicer A, de Almeida SD; Scourge Cohort Group; Riancho JA, Rojas-Martinez A, Flores C, Lapunzina P, Sánchez-Cabo F, Carracedo Á, Enriquez JA. Shaping current European mitochondrial haplogroup frequency in response to infection: the case of SARS-CoV-2 severity. Commun Biol. 2025 Jan 9;8(1):33. doi: 10.1038/s42003-024-07314-y. PMID: 39789223; PMCID: PMC11718132.

JACC CardioOncology

THE EUROPEAN MITOCHONDRIAL LINEAGE MAY PROTECT AGAINST SEVERE FORMS OF COVID-19

This study, led by Dr. Borja Ibáñez , and conducted in collaboration with international partners, presents a strategy for preventing the cardiotoxic effects of anthracyclines, a widely used class of anticancer drugs. Cardiotoxicity is a frequent adverse secondary effect of cancer therapy with these drugs. This study demonstrates that treatment with the SGLT2 inhibitor empagliflozin can mitigate the cardiac injury associated with anthracycline therapy.

Medina-Hernández D, Cádiz L, Mastrangelo A, Moreno-Arciniegas A, Fernández Tocino M, Cueto Becerra AA, Díaz-Guerra Priego A, Skoza WA, Higuero-Verdejo MI, López-Martín GJ, Pérez-Martínez C, de Molina-Iracheta A, Caballero-Valderrama M, Sánchez-González J, Sancho D, Fuster V, Galán-Arriola C, Ibáñez B. SGLT2i Therapy Prevents Anthracycline-Induced Cardiotoxicity in a Large Animal Model by Preserving Myocardial Energetics. JACC CardioOncol. 2025 Feb;7(2):171-184. doi: 10.1016/j.jaccao.2024.12.004. Epub 2025 Feb 4. PMID: 39967204; PMCID: PMC11866421.

Nature

CNIC SCIENTISTS DISCOVER A TYPE OF IMMUNE CELL THAT PRODUCES DEFENSIVE 'SHIELDS' IN THE SKIN

A team at the CNIC led by Dr. Andrés Hidalgo has discovered a specialized population of neutrophils in the skin that produce extracellular matrix, helping to maintain the skin's resistance and integrity. The study, published in Nature, demonstrates that the immune system not only targets pathogens for elimination, but also prevents them entering the body by physically strengthening the skin.

The study was supported by funding from Fundación "la Caixa", the Boehringer Ingelheim Foundation, the US National Institutes of Health, and the Swiss National Science Foundation.

Vicanolo T, Özcan A, Li JL, Huerta-López C, Ballesteros I, Rubio-Ponce A, Dumitru AC, Nicolás-Ávila JÁ, Molina-Moreno M, Reyes-Gutierrez P, Johnston AD, Martone C, Greto E, Quílez-Alvarez A, Calvo E, Bonzon-Kulichenko E, Álvarez-Velez R, Chooi MY, Kwok I, González-Bermúdez B, Malleret B, Espinosa FM, Zhang M, Wang YL, Sun D, Zhen Chong S, El-Armouche A, Kim KK, Udalova IA, Greco V, Garcia R, Vázquez J, Dopazo A, Plaza GR, Alegre-Cebollada J, Uderhardt S, Ng LG, Hidalgo A. Matrix-producing neutrophils populate and shield the skin. Nature. 2025 May;641(8063):740-748. doi: 10.1038/s41586-025-08741-5. Epub 2025 Mar 19. Erratum in: Nature. 2025 May;641(8065):E10. doi: 10.1038/s41586-025-09082-z. PMID: 40108463; PMCID: PMC12074881.

New England Journal of Medicine

A DRUG USED TO TREAT DIABETES IMPROVES THE PROGNOSIS OF PATIENTS UNDERGOING CARDIAC VALVE INTERVENTION

A drug used to treat diabetes improves the prognosis of patients with aortic stenosis treated by transcatheter aortic valve implantation (TAVI). The results of a clinical trial including 1,250 patients showed that medication with dapagliflozin after TAVI reduces the rates of death and hospital admission attributed to heart failure over a one-year follow-up period. The trial was coordinated by the CNIC and Hospital Álvaro Cunqueiro- Vigo.

The study received funding from the Carlos III Health Institute, the Spanish Society of Cardiology, the Galician Society of Cardiology, and the Castilla y León Regional Health Authority.

Raposeiras-Roubin S, Amat-Santos IJ, Rossello X, González Ferreiro R, González Bermúdez I, Lopez Otero D, Nombela-Franco L, Gheorghe L, Diez JL, Baladrón Zorita C, Baz JA, Muñoz García AJ, Vilalta V, Ojeda-Pineda S, de la Torre Hernández JM, Cordoba Soriano JG, Regueiro A, Bordes Siscar P, Salgado Fernández J, Garcia Del Blanco B, Martín-Reyes R, Romaguera R, Moris C, García Blas S, Franco-Peláez JA, Cruz-González I, Arzamendi D, Romero Rodríguez N, Díez-Del Hoyo F, Camacho Freire S, Bosa Ojeda F, Astorga Burgo JC, Molina Navarro E, Caballero Borrego J, Ruiz Quevedo V, Sánchez-Recalde Á, Peral Disdier V, Alegría-Barrero E, Torres-Llergo J, Feltes G, Fernández Díaz JA, Cuellas C, Jiménez Britez G, Sánchez-Rubio Lezcano J, Barreiro-Pardal C, Núñez-Gil I, Abu-Assi E, Iñiguez-Romo A, Fuster V, Ibáñez B; DapaTAVI Investigators. Dapagliflozin in Patients Undergoing Transcatheter Aortic-Valve Implantation. N Engl J Med. 2025 Apr 10;392(14):1396-1405. doi: 10.1056/NEJMoa2500366. Epub 2025 Mar 29. PMID: 40162639.

Circulation

THE HEART REMEMBERS: SCIENTISTS DESCRIBE HOW EARLY-LIFE CARDIAC INJURY IN PARENTS INFLUENCES THE DEVELOPMENT AND FUNCTION OF THE HEART IN THE NEXT GENERATION

Scientists at the CNIC and the University of Bern have found that heart surgery in male mice early in life creates a 'memory' that is passed on to the next generation. The study suggests that a parental history of heart surgery should be considered when evaluating cardiovascular health in descendants.

The study was supported by funding from the European Union Horizon 2020 Programme (grant 819719) and an interdisciplinary grant (UniBeAQ20 ID Grant) from the University of Bern.

- Coppe B, Galardi-Castilla M, Sanz-Morejón A, Arora P, Lucas J, Iciek C, Lalaguna L, Lara-Pezzi E, Flores I, Mercader N. Paternal Cardiac Lesion Induces Cardiac Adaptation in Offspring. Circulation. 2025 Apr;151(13):968-971. doi: 10.1161/CIRCULATIONAHA.124.070323. Epub 2025 Mar 31. PMID: 40163557.

Nature Communications

A TYPE OF IMMUNE CELL STRENGTHENS IMMUNOTHERAPY AND PREVENTS TUMOR RELAPSE IN ANIMAL MODELS

Scientists at the CNIC, working in collaboration with the Instituto de Investigación Biomédica de Barcelona (IRB Barcelona), have discovered a new immunotherapy strategy that reduces cancer recurrence in experimental mouse models. The study, shows that a specific subtype of immune cell—type I dendritic cells—is especially effective at activating a strong immune response and generating immune memory against cancer.

This study was supported with funding from the CNIC; the Ministerio de Ciencia, Innovación y Universidades (MICIU), the Agencia Estatal de Investigación, the European Union NextGenerationEU/PRTR; the Comunidad de Madrid; Fundación "la Caixa"; Asociación Española Contra el Cáncer; and Worldwide Cancer Research (25-0080).

- Heras-Murillo I, Mañanes D, Munné P, Núñez V, Herrera J, Catalá-Montoro M, Alvarez M, Del Pozo MA, Melero I, Wculek SK, Sancho D. Immunotherapy with conventional type-1 dendritic cells induces immune memory and limits tumor relapse. Nat Commun. 2025 Apr 9;16(1):3369. doi: 10.1038/s41467-025-58289-1. PMID: 40204706; PMCID: PMC11982544.

Circulation Research

BREAKTHROUGH GENE THERAPY OFFERS HOPE FOR RARE, DEADLY HEART DISEASE IN YOUNG MEN

The CNIC team led by Dr. Enrique Lara-Pezzi has developed an innovative gene-therapy strategy that could transform the treatment of arrhythmogenic right ventricular cardiomyopathy type 5 (ARVC5), a rare and highly penetrant inherited cardiac disorder with an elevated risk of sudden cardiac death. This disease is particularly devastating in young men and lacks a cure, with current treatments focusing on palliative care.

The study was supported by the Pathfinder Cardiogenomics program of the European Innovation Council (project DCM-NEXT; 101115416); grants PID2021-124629OB-I00, TED2021-129774B-C22, and PLEC2022-009235 from the Ministerio de Ciencia e Innovación (MCIN/ AEI/10.13039/501100011033); the European Union NextGenerationEU/PRTR; and the European Regional Development Fund.

- Lalaguna L, Arévalo-Núñez de Arenas M, López-Olañeta M, Villalba-Orero M, Jiménez-Riobóo RJ, Gómez-Gaviro MV, Isern J, Muñoz-Cánoves P, Byrne BJ, Ochoa JP, García-Pavía P, Lara-Pezzi E. Overexpression of Wild-Type TMEM43 Improves Cardiac Function in Arrhythmogenic Right Ventricular Cardiomyopathy Type 5. Circ Res. 2025 Apr 11;136(8):830-844. doi: 10.1161/CIRCRESAHA.124.325848. Epub 2025 Mar 17. PMID: 40091736; PMCID: PMC11984551.

Nature Biomedical Engineering

A NEW METHOD FOR STUDYING MECHANICAL PROTEINS AND THEIR INVOLVEMENT IN MUSCULAR DISORDERS

A team at the CNIC led by Dr. Jorge Alegre-Cebollada has developed an innovative method, called TEVs-TTN, for studying the specific mechanical functions of proteins through their controlled cleavage, a process that renders the proteins unable to sense and transmit mechanical force. The findings extend knowledge about the development of muscular diseases. This study demonstrates that interrupting mechanical transmission by the protein titin triggers the development of muscular diseases. This finding opens new routes to understanding muscular dystrophies and other diseases associated with the protein titin.

The study was funded mainly by the European Resarch Council through the ProtMechanics-Life Consolidator Grant (101002927) and a postdoctoral fellowship from the European Molecular Biology Organization to Dr. Silva-Rojas (EMBO ALTF 417-2022).

- Silva-Rojas R, Vicente N, Gavilán-Herrera M, Labrador-Cantarero V, Sicilia J, Giménez-Sáez O, Dumitru AC, Sánchez MI, Gato-Vilaseca M, Velázquez-Carreras D, López JA, Vázquez J, Herrero-Galán E, López-Unzu MA, Pricolo MR, Alegre-Cebollada J. Mechanically knocking out titin reveals protein tension loss as a trigger of muscle disease. Nat Biomed Eng. 2025 Oct;9(10):1758-1774. doi: 10.1038/s41551-025-01403-x. Epub 2025 Jun 5. PMID: 40473933.

Circulation Research

CNIC SCIENTISTS UNCOVER HOW THE IMMUNE RESPONSE DRIVES ATHEROSCLEROSIS—THE ROOT CAUSE OF HEART ATTACKS AND STROKES

CNIC scientists, in collaboration with national and international research centers, have identified a key immune cell subtype involved in the development of atherosclerosis. The team tested an experimental therapy in animal models based on immunosuppressive nanoparticles and demonstrated that it can slow disease progression.

The project was supported by funding from the Spanish Ministry of Science, Innovation, and Universities (MICIU): PID2022-137712OB-I00, PID2021-123238OB-I00, PID2022-139218OB-I00, CNS2023-143944, RYC2020-030241-I, PID2022-142842OB-I00, CPP2021-008310 and CPP2022-009762, funded by the State Research Agency and the European Union NextGeneration EU/PRTR. Additional funding was provided by the Community of Madrid (P2022/BMD-7333 INMUNOVAR-CM) and Fundación "la Caixa" (LCF/PR/HR23/52430012 and LCF/PR/HR22/52420019).

- Galán M, Fernández-Méndez L, Núñez V, Femenía-Muiña M, Figuera-Belmonte P, Moya-Ruiz E, Martínez-Cano S, Hernández-García E, Rodrigo-Tapias M, Rodríguez-Ronchel A, Relaño-Rupérez C, Wculek SK, Benguria A, Dopazo A, Henri S, Jo S, Liu TT, Malissen B, Murphy KM, Ramiro AR, Carregal-Romero S, Ruiz-Cabello J, Robles-Vera I, Sancho D. cDC1s Promote Atherosclerosis via Local Immunity and Are Targetable for Therapy. Circ Res. 2025 Jul 18;137(3):400-416. doi: 10.1161/CIRCRESAHA.124.325792. Epub 2025 May 30. PMID: 40444360; PMCID: PMC12272919.

Science Translational Medicine

A HOSPITAL IMAGING TECHNIQUE USED IN CANCER CARE IMPROVES THE MONITORING AND TREATMENT OF ATHEROSCLEROSIS

Scientists at the CNIC have shown that 18FDG-PET, an imaging technique widely used to study other conditions, can also be used to monitor atherosclerosis by measuring cellular metabolism within arterial plaques. These findings could improve the clinical management of this disease and accelerate the development of new treatments.

The study received funding from the ERC under the European Union's Horizon 2020 research and innovation programme; the Spanish Ministry of Economy, Industry, and Competitiveness (MEIC), with co-funding from ERDF; the Instituto de Salud Carlos III, with ERDF/EU co-funding; the Madrid regional government; and Fundación "la Caixa" (AtheroConvergence).

- Nogales P, Velasco C, González-Cintado L, Sharysh D, Mota-Cobián A, Izquierdo-Serrano R, Torroja C, Del Rio-Aledo D, Morales-Cano D, Mota RA, Benguría A, Dopazo A, Sánchez-Cabo F, Vázquez J, España S, Carramolino L, Mateo J, Bentzon JF. Atherosclerotic disease

activity is associated with glycolytic enzyme expression across multiple cell types and is trackable by FDG-PET. Sci Transl Med. 2025 Aug 13;17(811):eado6467. doi: 10.1126/scitranslmed.ado6467. Epub 2025 Aug 13. PMID: 40802740.

European Heart Journal

GENES LINKED TO SUDDEN CARDIAC DEATH INCREASE THE RISK OF HEART FAILURE IN PATIENTS WITH GENETIC DILATED CARDIOMYOPATHY

A study led by Dr. Pablo García-Pavía and Dr. Fernando Domínguez—investigators at the CNIC and cardiologists at Hospital Universitario Puerta de Hierro and CIBERCV—shows that patients with genetic dilated cardiomyopathy who experience severe arrhythmias are at an elevated risk of developing advanced heart failure and requiring a heart transplant. The study was conducted through collaboration among 19 Spanish hospitals and the analysis of more than 1,200 patients.

This study received funding from the Instituto de Salud Carlos III (PI20/0320) with ERDF co-funding and the Pathfinder Cardiogenomics Programme of the European Union's European Innovation Council (project DCM-NEXT; project 101115416).

- Mora-Ayestarán N, Ochoa JP, Gómez-González C, Navarro-Peñalver M, Gallego-Delgado M, Larrañaga-Moreira JM, Robles-Mezcua A, Basurte-Elorz MT, Rodriguez-Palomares JF, Climent-Paya V, Jiménez-Jaímez J, Mogollón-Jiménez MV, García-Granja PE, García-Álvarez A, Peña-Peña ML, Alvarez Barredo M, Ripoll-Vera T, Palomino-Doza J, Bayes-Genis A, Tirón C, Fernández AI, Sabater-Molina M, Toranzo I, Crespo-Leiro MG, Doncel-Abad V, Lacuey-Lecumberri G, Limeres-Freire J, García-Álvarez MI, Cabrera-Borrego E, Kounka-Ait El Maalem Z, Vilches S, González-López E, Villacorta E, García-Pinilla JM, Barriales-Villa R, Gimeno-Blanes JR, Garcia-Pavia P, Domínguez F. Arrhythmic genotypes in dilated cardiomyopathy and risk of advanced heart failure. Eur Heart J. 2025 Dec 22;46(48):5222-5233. doi: 10.1093/eurheartj/ehaf605. PMID: 40878535; PMCID: PMC12718688.

New England Journal of Medicine & The Lancet

CNIC-LED REBOOT CLINICAL TRIAL CHALLENGES 40-YEAR-OLD STANDARD OF CARE FOR HEART ATTACK PATIENTS

The REBOOT study, coordinated by the CNIC together with the Mario Negri Institute in Milan, shows that beta-blockers do not benefit patients who survive an uncomplicated myocardial infarction while maintaining normal cardiac function. The finding challenges established medical practice in place for more than four decades.

The results, published simultaneously in *The New England Journal of Medicine* and *The Lancet*, and presented at the *European Society of Cardiology (ESC) Congress* in Madrid, mark a paradigm shift in post-heart attack treatment.

Funded by the CNIC, the study results simplify and optimize post-heart attack treatment, reducing side effects and improving patients' quality of life.

- Ibanez B, Latini R, Rossello X, Dominguez-Rodriguez A, Fernández-Vazquez F, Pelizzoni V, Sánchez PL, Anguita M, Barrabés JA, Raposeiras-Roubín S, Pocock S, Escalera N, Staszewsky L, Pérez-García CN, Díez-Villanueva P, Pérez-Rivera JA, Prada-Delgado O, Owen R, Pizarro G, Caldes O, Gómez-Talavera S, Tuñón J, Bianco M, Zarauza J, Vetrano A, Campos A, Martínez-Huertas S, Bueno H, Puentes M, Grigis G, Bonilla-Palomas JL, Marco E, González-Juanatey JR, Bangueses R, González-Juanatey C, García-Álvarez A, Ruiz-García J, Carrasquer A, García-Rubira JC, Pascual-Figal D, Tomás-Querol C, San Román JA, Baratta P, Agüero J, Martín-Reyes R, Colivicchi F, Ortas-Nadal R, Bazal P, Cordero A, Fernández-Ortiz A, Basso P, González E, Poletti F, Bugani G, Debiasio M, Cosmi D, Navazio A, Bermejo J, Tortorella G, Marini M, Botas J, de la Torre-Hernández JM, Ottani F, Fuster V; REBOOT-CNIC Investigators. Beta-Blockers after Myocardial Infarction without Reduced Ejection Fraction. N Engl J Med. 2025 Nov 13;393(19):1889-1900. doi: 10.1056/NEJMoa2504735. Epub 2025 Aug 30. PMID: 40888702.
- Rossello X, Prescott EIB, Kristensen AMD, Latini R, Fuster V, Fagerland MW, Pocock SJ, Halvorsen S, Dominguez-Rodriguez A, Holmager TLF, Sanchez PL, Bakken A, Raposeiras-Roubin S, Jensen SE, Kimura T, Ottani F, Lambrechtsen J, Anguita M, Ozasa N, Atar D, Ibanez B, Munkhaugen J. β blockers after myocardial infarction with mildly reduced ejection fraction: an individual patient data meta-analysis of randomised controlled trials. Lancet. 2025 Sep 13;406(10508):1128-1137. doi: 10.1016/S0140-6736(25)01592-2. Epub 2025 Aug 30. PMID: 40897190.

European Heart Journal

A NEW STUDY FINDS THAT, AFTER A HEART ATTACK, WOMEN HAVE A WORSE PROGNOSIS WHEN TREATED WITH BETA-BLOCKERS

The REBOOT study, coordinated by the CNIC and presented at the 2025 ESC Congress, revealed important sex-specific differences in beta-blocker therapy after myocardial infarction in patients with preserved cardiac function. While men showed no benefit or harm, women with fully normal heart function (LVEF ≥ 50%) faced higher risks of death, reinfarction, or heart failure when treated with beta-blockers.

The REBOOT clinical trial, funded by the CNIC, was carried out through collaboration with the Spanish Society of Cardiology (SEC) and CIBERCV.

- Rossello X, Dominguez-Rodriguez A, Latini R, Sánchez PL, Raposeiras-Roubín S, Anguita M, Barrabés JA, Grigis G, Owen R, Pocock S, Gómez-Talavera S, García-Lunar I, Escalera N, Pérez-García CN, Di Fusco SA, Pizarro G, López Benito M, Pongetti G, Rincón-Díaz LM, Buera I, Rozado J, García MJ, Prada-Delgado O, Cosmi D, Fuster V, Ibanez B. Beta-blockers after myocardial infarction: effects according to sex in the REBOOT trial. Eur Heart J. 2025 Aug 30:ehaf673. doi: 10.1093/eurheartj/ehaf673. Epub ahead of print. PMID: 40884211.

European Heart Journal

CNIC SCIENTISTS REPORT THE FIRST USE OF CRISPR ACTIVATION TO TREAT A CARDIAC DISEASE IN A MOUSE MODEL

An international multidisciplinary team led by the CNIC, with participation from scientists at Hospital Universitario Puerta de Hierro and the University of California San Diego, has demonstrated that CRISPR-based gene activation (CRISPRa) can be used to treat genetic heart disease *in vivo*. This study, presented at the ESC Congress in Madrid, paves the way for novel targeted therapies for patients with genetic cardiac disorders. This approach could be especially useful for patients with conditions caused by mutations in genes too large to be targeted with conventional gene therapy.

The study was funded by the Spanish Ministry of Science, Innovation, and Universities, the Spanish cardiovascular research network (CIBERCV), and the European Innovation Council of the European Union.

- Cañas-Alvaro R, Lalaguna L, Rubio B, Ausiello A, López-Olañeta M, Serrano-Blanco RF, Ochoa JP, de la Pompa JL, Chavez A, García-Pavía P, Lara-Pezzi E. CRISPR activation to repair electrocardiogram abnormalities caused by a FLNC truncating variant in mice. Eur Heart J. 2025 Nov 14;46(43):4610-4613. doi: 10.1093/eurheartj/ehaf703. PMID: 40886060; PMCID: PMC12614992.

Developmental Cell

A CNIC TEAM REVEALS HOW THE HEART IS ORGANIZED FROM THE EARLIEST STAGES OF EMBRYONIC DEVELOPMENT

A study published in *Developmental Cell* uncovered new insights into how the heart forms during the earliest stages of embryonic development. The research, led by scientists at the CNIC, shows that the heart originates from two distinct cell populations that form independently—but in a coordinated manner—from the onset of gastrulation, the early developmental process in which the embryo begins to organize its basic cellular layers.

The study was funded by Fundación "la Caixa" (ID 100010434), the Company of Biologists, the Spanish State Research Agency, the European Commission H2020 programme REANIMA, and CARDIOBOOST-CM from the Community of Madrid. It also received support from the ERDF (ReDIB ICTS TRIMA@CNIC infrastructure, MCIN).

- Sendra M, McDole K, de Dios Hourcade J, Temiño S, Raiola M, Guignard L, Keller PJ, Domínguez JN, Torres M. Myocardium and endocardium of the early mammalian heart tube arise from independent multipotent lineages specified at the primitive streak. Dev Cell. 2025 Sep 22;60(18):2434-2444.e5. doi: 10.1016/j.devcel.2025.05.002. Epub 2025 May 27. PMID: 40436021; PMCID: PMC7618247.

New England Journal of Medicine

MAJOR INTERNATIONAL STUDY CONFIRMS THAT BETA-BLOCKERS ARE NO LONGER NEEDED IN POST-INFARCTION PATIENTS WITH NORMAL HEART FUNCTION

This landmark meta-analysis, presented at the 2025 American Heart Association Congress, concludes that beta-blockers do not reduce death, recurrent heart attack, or heart failure in patients who experience a myocardial infarction but maintain normal cardiac function (ejection fraction ≥50%). Led by the CNIC, the study pooled individual data from 17,801 patients across five major clinical trials—REBOOT, REDUCE-AMI, BETAMI, DANBLOCK, and CAPITAL-RCT—representing the most comprehensive analysis to date. The results showed no clinical benefit from beta-blocker therapy in this population, regardless of age, sex, or type of drug used.

The study was supported by funding from the CNIC, the Swedish Heart and Lung Foundation, Region Stockholm, the South-Eastern Norway Regional Health Authority; Research Council of Norway, the Danish Heart Foundation, Novo Nordisk Foundation, and the Research Institute for Production Development in Kyoto.

- Kristensen AMD, Rossello X, Atar D, Yndigegn T, Kimura T, Latini R, Lindahl B, Halvorsen S, Olsen MH, Fuster V, Hofmann R, Vikenes K, Maeng M, Erlinge D, Pocock S, Karlström P, Bakken A, Lange T, Barrabés JA, Benatar J, Raposeiras-Roubin S, Held C, Piepoli M, Fagerland MW, Holmager T, Ozasa N, Prescott EIB, Munkhaugen J, Jernberg T, Ibanez B; Beta-Blocker Trialists' Collaboration Study Group. Beta-Blockers after Myocardial Infarction with Normal Ejection Fraction. N Engl J Med. 2025 Nov 9. doi: 10.1056/NEJMoa2512686. Epub ahead of print. PMID: 41211954.

Journal of Experimental Medicine

NEUTROPHILS ARE LESS AGGRESSIVE AT NIGHT, EXPLAINING WHY NIGHTTIME HEART ATTACKS CAUSE LESS DAMAGE THAN DAYTIME EVENT

A CNIC study explains why heart attacks that occur at night are less severe than those that strike during the day. The study, led by Dr. Andrés Hidalgo's group at the CNIC, shows that neutrophils—a type of white blood cell—have an internal clock that regulates their aggressiveness throughout the day and determines the extent of damage they cause to the heart after a heart attack. The researchers also developed a pharmacological strategy in experimental models to block the molecular clock in neutrophils, keeping them in a 'nighttime' state and thereby reducing their harmful potential during a heart attack.

The study was supported by funding from Fundación La Caixa; the US National Institutes of Health (NIH); the Spanish Ministry of Science, Innovation, and Universities (MICIU); the China Scholarship Council; ANR PRC; Fondation pour la Recherche Médicale (FRM); the Leducq Transatlantic Network of Excellence on circadian effects in stroke; the Spanish Society of Cardiology; and support from AstraZeneca, Boehringer Ingelheim, and Janssen.

- Aroca-Crevillén A, Martín-Salamanca S, Torres LS, Crainiciuc G, Sicilia J, Peñaloza-Martínez E, Rosillo N, Molina-Moreno M, Adrover JM, Rubio-Ponce A, Vicanolo T, Liu X, Wichapong K, Núñez V, Balabanian K, Bachelerie F, Sancho D, Casanova-Acebes M, Ortiz-Pérez JT, Moro MÁ, Bueno H, Nicolaes GAF, Hidalgo A. A circadian checkpoint relocates neutrophils to minimize injury. J Exp Med. 2026 Feb 2;223(2):e20250240. doi: 10.1084/jem.20250240. Epub 2025 Dec 12. PMID: 41385080; PMCID: PMC7618653.

4 CNIC News and Views

Back to Contents

1. Visiting Scientists

Spain's growing international profile in scientific research makes it an increasingly attractive destination for visiting scientists from around the world.

Fundación Occident Visiting Researchers Program

Since 2013, the CNIC and *Fundación Occident* have worked together to bring international scientists to the CNIC through the *Fundación*'s Visiting Researchers Program. The program supports research visits to Spanish institutions, with the aim of building inter-institutional ties and opening new lines of research.

Three research-visit proposals were approved in 2025:

1. **Dr. Francesco Costa**, Professor at the University of Messina, Italy; Interventional Physician at Virgen de la Victoria Hospital in Málaga; and Researcher at the Málaga Biomedical Research Institute and Nanomedicine Platform, Spain.

2. **Dr. Anthony Firulli**, Director of the Cardiac Developmental Biology Program at the Herman B. Wells Center for Pediatric Research, Riley Heart Research Center, Indiana University School of Medicine, Indianapolis, USA.

3. **Dr. Stepan Heymans**, Chair of the Heart Failure Research Centre and the Clinical Cardiomyopathy Program at Maastricht UMC, Netherlands, and Professor of Inflammation & Matrix Biology at the University of Leuven, Belgium.

In September 2025, Dr. Costa began his collaboration with the CNIC, working in the group led by Dr. Borja Ibáñez. His stay that will continue until September 2026.

2. Awards and Honours

CNIC General Director Dr. Valentín Fuster received the following awards and recognitions in 2025.

***Orden de Duarte, Sánchez y Mella* — the Dominican Republic's highest distinction**

The Dominican Republic honored Dr. Valentín Fuster with the *Orden de Duarte, Sánchez y Mella*, the country's highest order of merit, awarded for distinguished service, outstanding achievements, contributions to humanity, scientific discoveries, exceptional works of art, and other noteworthy accomplishments.

Doctor Honoris Causa and Presidential Honorary Award in Cyprus

During an official ceremony, the President of Cyprus, Nikos Christodoulides, presented Dr. Fuster with the Presidential Honorary Award, acknowledging his outstanding contributions to cardiovascular health and his lifelong commitment to advancing medical science. The European University of Cyprus also awarded Dr. Fuster the title of Doctor Honoris Causa, a distinction reserved for individuals whose scientific achievements and dedication have had a profound impact on society.

Tribute to Dr. Valentín Fuster at Fundación Jiménez Díaz

Dr. Fuster was a featured speaker at the lecture series organized by *Fundación Jiménez Díaz* (FJD) to celebrate its 90th Anniversary. Nearly 300 attendees gathered in the hospital's Aula Magna to hear Dr. Fuster reflect on his personal and professional journey. In a conversation with CNIC Scientific Director and FJD cardiologist Dr. Borja Ibáñez, Dr. Fuster spoke about medical vocation, the value of mentors, and the need for a more human approach to medicine.

Dr. Miguel Torres receives the 2025 National Genetics Award
The Spanish Genetics Society (SEG) awarded Dr. Miguel Torres Sánchez with the 2025 National Genetics Award in the applied category, recognizing his contributions to the development of regenerative therapies for the heart.

Dr. Jorge Alegre-Cebollada named recipient of the 2026 Michael and Kate Bárány Prize
The Biophysical Society named Jorge Alegre-Cebollada recipient of the 2026 Michael and Kate Bárány Award for his pioneering studies of protein mechanics in living systems, revealing how mechanical forces govern protein function and contribute to human disease.

Dr. Vicente Andrés and Dr. Ana Barettino honored in the inaugural awards of the Chair of Rare Diseases at the University of Almería
Dr. Vicente Andrés was honored for the Best Scientific Publication and Dr. Ana Barettino received a special mention for her doctoral thesis in the inaugural awards of the Chair of Rare Diseases at the University of Almería. The awards aim to promote research, raise awareness of the social and healthcare impact of rare diseases, and foster public understanding.

Dr. Silvia G. Priori awarded the 2025 Valentin Fuster Award for Innovation in Science by the American College of Cardiology
Dr. Priori was recognized alongside other 2025 Distinguished Award winners at the American College of Cardiology's Annual Scientific Session (ACC.25), held March 29-31, 2025, in Chicago

Dr. Agustín Clemente Moragón receives a CSIC Outstanding Doctoral Thesis Award
Dr. Agustín Clemente Moragón, a member of the Translational Laboratory for Cardiovascular Imaging and Therapy led by Dr. Borja Ibáñez, received a Relevant Doctoral Thesis Award from the Spanish National Research Council (CSIC).
These awards recognized theses defended in 2023 and 2024 that stood out for their quality, impact, and scientific relevance. Dr. Clemente Moragón carried out his thesis under the supervision of Drs. Borja Ibáñez and Eduardo Oliver, and defended at at the UAM on 24 February 2023. Titled "Translational and Mechanistic Study about Beta-1-Adrenergic Receptor Modulation on Neutrophils as a Therapy against Ischemia/Reperfusion Injury," the work examines a potential therapeutic approach to a major challenge in cardiac care.

CNIC research into cardiotoxicity in cancer awarded the AECC prize for best scientific article

Anabel Díaz-Guerra received the prize for the best scientific article published in 2024 by recipients of AECC pre-doctoral grants. Her article, *Anthracycline Cardiotoxicity Induces Progressive Changes in Myocardial Metabolism and Mitochondrial Quality Control: Novel Therapeutic Target*, was published in JACC: Cardioncology, 6, 217-232.

FECYT awarded quality certification to REPISALUD

The Spanish Foundation for Science and Technology (FECYT) awarded its quality certification to REPISALUD, the institutional repository of the *Instituto de Salud Carlos III* (ISCIII) and its foundations—the CNIC and CNIO.

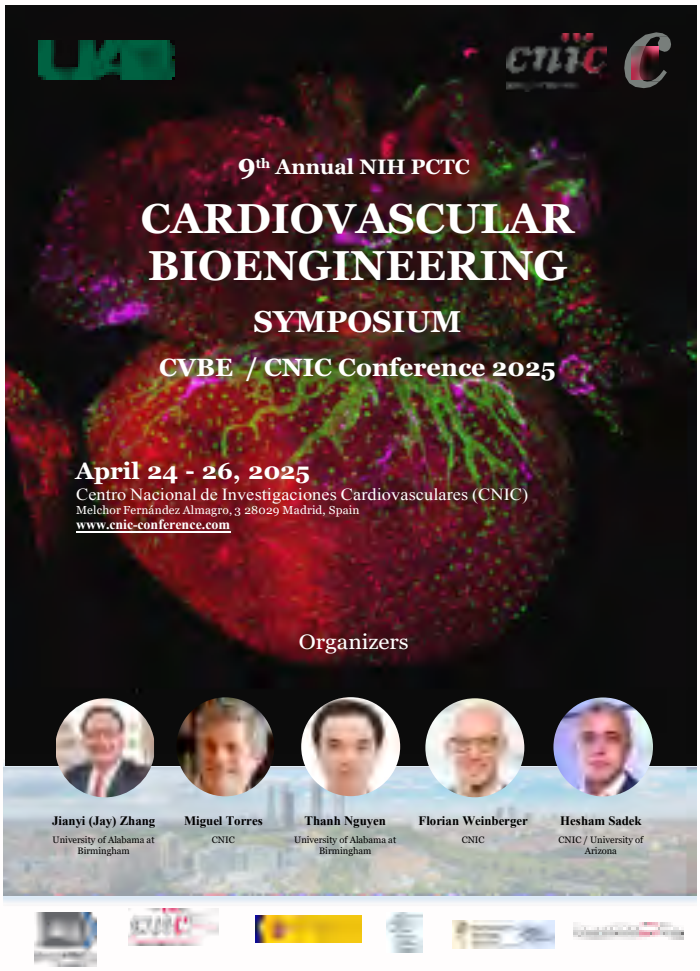
CNIC research featured on the cover of National Geographic Spain

The November 2025 issue of the Spanish edition of *National Geographic* magazine dedicated its cover story to the heart and the latest advances in cardiology, with a prominent focus on the CNIC.

3 Scientific Events

CNIC Conference: 9th Annual Cardiovascular Bioengineering Symposium

The 9th Annual Cardiovascular Bioengineering Symposium, organizers by the CNIC and the National Institutes of Health (USA), highlighted cutting-edge research in stem-cell biology, cardiac regeneration, vascular biology, metabolism, and cardiology. The meeting was held in the CNIC Auditorium.



The CNIC at the European Society of Cardiology Congress

The CNIC played a prominent role at the European Society of Cardiology Congress (ESC Congress 2025 August 29-September 1), held in Madrid. CNIC experts led scientific sessions, presented high-impact studies and consensus documents, and received international recognition, reinforcing the center's standing as a leading institution in cardiovascular research.

Held under the theme "Global Health: cardiology without borders," the congress brought together thousands of professionals to address global cardiovascular health challenges and discuss the latest scientific and clinical advances.

CNIC General Director Dr. Valentín Fuster was selected by the World Heart Federation (WHF) to deliver the Inaugural Lecture at the WHF World Congress of Cardiology, held within the ESC Congress. This distinction—awarded by the WHF for the first time—recognizes individuals with exceptional contributions to global cardiovascular health.

Cardiovascular health with a gender perspective: experts from 21 European countries gather in Madrid for the JACARDI General Assembly

The CNIC hosted the Third General Assembly of JACARDI, the major European initiative to improve the prevention and treatment of cardiovascular disease and diabetes, with gender and health equity at the center of the agenda.

The Assembly brought together more than 200 representatives from 21 European countries, along with spokespersons from the European Commission, the WHO Regional Office for Europe, scientific societies, and patient organizations. Key themes included gender equity, sustainability, data monitoring, and the upcoming EU Cardiovascular Health Plan.

CNIC co-hosts CardioTox 25, the leading international congress on cardiovascular health in cancer patients

The CNIC hosted opening sessions of CardioTox 25 on November 4, with Hospital La Paz hosting subsequent sessions on November 5 and 6. CardioTox is the leading international meeting dedicated to cardiovascular health in cancer patients. As in previous editions, the event brought together professionals from multiple disciplines—including oncology, hematology, cardiology, primary care, nursing, and other health fields—with a shared goal: optimizing cardiovascular care across the cancer journey. The meeting was chaired by cardiologist Dr. Teresa López-Fernández, who also participates in CNIC-coordinated research projects.

PHDAY: Stronger Science, Healthier Lives

Held on Friday November 28 under the title "*Stronger Science, Healthier Lives*," explored the impact of science on cardiovascular health and how cutting-edge research is shaping the future of medicine. The event brought together experts from multiple fields to discuss the latest advances in cardiology, lifestyle interventions, and aging, while offering more than 170 early-career researchers prticipants valuable networking and learning opportunities. More information at https://phday.cnic.es/.

CNIC and the Ramón Areces Foundation organize the international symposium "Understanding the Neurovascular Network to Prevent Dementia"

Held on December 4, 2024, at the Ramón Areces Foundation Auditorium, this symposium addressed one of the greatest global health challenges of the 21st century. Recent research highlights the essential role of the neurovascular network—encompassing cerebral blood flow, the blood–brain barrier, and the brain's drainage systems—in maintaining cognitive function and brain health.

The meeting brought together leading international experts to address, from a multidisciplinary perspective, the neurovascular mechanisms that contribute to cognitive decline. It was coordinated by CNIC General Director Valentín Fuster; Costantino Iadecola, Director of the Feil Family Brain and Mind Research Institute at Weill Cornell Medicine (New York); Marta Cortés-Canteli, from the Cajal Center for Neuroscience (CSIC); and María Ángeles Moro, Coordinator of the CNIC Program on Cardiovascular Risk Factors and Brain Health.

Cardiovascular health with a gender perspective: experts from 21 European countries gather in Madrid for the JACARDI General Assembly

The CNIC hosted the Third General Assembly of JACARDI, the major European initiative to improve the prevention and treatment of cardiovascular disease and diabetes, with gender and health equity at the center of the agenda.

The Assembly brought together more than 200 representatives from 21 European countries, along with spokespersons from the European Commission, the WHO Regional Office for Europe, scientific societies, and patient organizations. Key themes included gender equity, sustainability, data monitoring, and the upcoming EU Cardiovascular Health Plan.

4. Grants

Three CNIC projects receive more than €5 million in ERC Advanced Grant funding

Three CNIC projects received European Research Council (ERC) Advanced Grant funding from the European Commission. ANTI-ATHERO: *Age-Associated Antigens in Atherosclerosis Immunity and Immunotherapy*, led by Dr. Almudena Ramiro, and MINTRAF: *Cell-Cell Communication by Mitochondrial Intercellular Traffic*, led by Dr. José Antonio Enríquez, will each receive €2.5 million over the next 5 years.

A further €2.5 million was awarded to Nab-Heart: *Nanobody-Targeted Camk2d Inhibition for Cardiac Arrhythmia*, led by Dr. Silvia Priori, professor of cardiology at the University of Pavia (Italy) and head of the CNIC Molecular Cardiology Group. Of the total, €250,000 is assigned to her CNIC group.

CNIC joins GRACE, a European project to transform cardiovascular care through innovation

The CNIC has been allocated €405,625 for its involvement in GRACE, a project focused on developing innovative strategies to improve the detection and management of cardiovascular diseases.

Two Marie Skłodowska-Curie grants awarded to CNIC researchers

Dr. Pablo Rodríguez Silvestre will study the influence of fatty-acid oxidation on the immune response, while Dr. Jennifer Monereo Sánchez will investigate the relationship between brain health, atherosclerosis, and cardiovascular risk.

Two CNIC projects selected in the 2025 "la Caixa" Foundation Health Research funding round

The two CNIC projects were among 34 cutting-edge biomedical research projects selected from a total of 714 proposals:

The Legacy of Anthracyclines in Bone Marrow and Long-Term Cardiovascular Risks in Cancer Survivors, led by Dr. Borja Ibáñez

Improving Gene Therapy for Life-Threatening Heart Diseases, led by Dr. Juan Bernal.

Isabel Gemio Foundation awards €60,000 to CNIC research project led by Henar Cuervo
Fundación Isabel Gemio awarded a €60,000 grant to the project "Identification and Characterization of Key Factors in the Progression of Arteriovenous Malformations," led by Dr. Henar Cuervo of the Molecular Genetics of Angiogenesis Research Group at the CNIC.

5. Outreach Activities

International Day of Women and Girls in Science
On February 11, the CNIC organized a special morning event to mark the International Day of Women and Girls in Science, aimed at promoting scientific vocations and raising visibility of the role of women in STEM.

The event opened with a video introducing students to the professional and personal journeys of several CNIC researchers, followed by a roundtable discussion on the role of women in research, the barriers that persist in scientific careers, and the opportunities to drive meaningful change.

International Women's Day and European Day for the Prevention of Cardiovascular Risk
To mark International Women's Day (March 8) and the European Day for the Prevention of Cardiovascular Risk (March 14), the CNIC organized a public event on the afternoon of March 13 focused on cardiovascular risk prevention in women.

Dr. Maria Rubini, cardiologist, CNIC researcher, and chair of the Gender Working Group of the European Society of Cardiology (ESC), participated in "*A WakeUp Call: Key Trends and Policy Issues in Cardiovascular Health for Women and Girls*," organized in the European Parliament in collaboration with the ESC. Her presentation, "Shedding Light on Cardiovascular Disease in Women and the Need for Action," highlighted the importance of raising awareness of cardiovascular disease in women.

European Researchers' Night

On Friday, September 26 the CNIC took part in the 16th edition of the European Researchers' Night, joining this European Commission initiative held simultaneously in more than 350 cities across Europe. The CNIC organized twelve outreach activities designed to bring participants closer to the Center's research, engaging audiences of all ages through workshops, guided visits, hands-on experiments, talks, and demonstrations.

Topics ranged from rare diseases and cardiac physiology to neuroscience, DNA extraction, PCR, nutrition and lifestyle, blood-flow dynamics, and an immersive virtual-reality experience on drug design.

World Heart Day

The CNIC, with the collaboration of Dr. Borja Ibáñez reaffirmed its commitment to the detection, treatment, and prevention of cardiovascular diseases—and reminded the public that heart health also depends on everyday choices. Healthy lifestyle habits can prevent most cardiovascular diseases, which remain the leading cause of death worldwide. The CNIC's key recommendations:

- Maintain a balanced diet rich in fruits, vegetables, and legumes, and low in saturated fats and sugars.
- Engage in regular physical activity—at least 30 minutes a day.
- Avoid tobacco and minimize alcohol consumption.
- Monitor risk factors such as high blood pressure, cholesterol, and diabetes through regular check-ups.
- Take care of your mental health, get enough sleep, and manage stress.

Science and Innovation Week

As part of the 26th Science and Innovation Week 2025 , held November 4 to 16, the CNIC organized twenty-one activities to showcase its research and bring science to people of all ages. Through hands-on hands on experiments, workshops, demonstrations, and talks, participants engaged with recent discoveries and technological advances across a wide range of topics: cell fate, cardiovascular physiology, genetics, neuroscience, cancer-heart interactions, rare diseases, adolescent cardiovascular health, molecular biology, and interactive formats including escape rooms and virtual-reality experiences.

6. Social and CNIC

CNIC receives a donation to research Hutchinson-Gilford progeria syndrome

The Molecular Cardiovascular Physiopathology and Genetics Laboratory, headed by Dr. Vicente Andrés, received a donation of €10,000 from the Alexandra Peraut Progeria Association, raised at a fundraising gala last March. The funds will support research on Hutchinson-Gilford progeria syndrome (HGPS), an ultra-rare genetic disease affecting approximately 1 in 20 million people.

CNIC obtains the *Equality in the Workplace* distinction from the Women's Institute

The *Equality in the Workplace* distinction is a mark of excellence recognizing organizations that excel in implementing equality plans and policies across areas such as access to employment, working conditions, work-life balance, shared responsibility, equal pay, inclusive communication, organizational model, and social responsibility. It is governed by Royal Decree 1615/2009, as recently amended by Royal Decree 333/2023.

Dr. Vicente Andrés, Director of Basic Research at the CNIC, accepted the award at a ceremony held as part of a conference organized by the Women's Institute—an autonomous body attached to the Ministry of Equality, chaired by Minister of Equality Ana Redondo—under the slogan "Breaking Barriers, Multiplying Talent."

Through its Equality Plan, the CNIC promotes and disseminates the principle of equality, ensures the implementation of ethical codes and procedures that support it, and applies policies to prevent all forms of discrimination in recruitment, wages, risk prevention, and work-life balance. These commitments also extend to all activities involving third parties—includingpublic tenders and agreements—through specific gender impact reports.

CNIC participates in the 16th Popular Heart Race to promote cardiovascular prevention

On Saturday, September27, the CNIC participated in the 16th Heart Popular Race, organized by the Spanish Heart Foundation. The event brought together thousands of participants united by a shared goal: raising awareness of the importance of physical activity in preventing cardiovascular disease. The CNIC's participation reflects its ongoing commitment to healthy lifestyle habits and public cardiovascular health.

5 Training Programs

Back to Contents

Training is one of the CNIC's core activities, and the Center has devised a comprehensive training plan, the CNIC-Joven Training Plan, which includes programs for participants at all levels, from high-school students to postdoctoral researchers and MDs (https://www.cnic.es/en/training-cnic). The CNIC-Joven Training Plan aims to fulfill Valentín Fuster's personal goal "to attract and train the brightest young people from the earliest ages to create a pool of researchers of excellence in the field of cardiovascular research."

HIGH SCHOOL STUDENTS INTERNSHIPS

ACERCATE PROGRAM

The Acércate Program provides top-performing senior high school graduates in the Science and Technology track a unique opportunity to immerse themselves in the world of biomedical research. Through a rigorous national selection process, the program identifies talented students who then participate in learning experiences designed to ignite and nurture their passion for biomedical science.

Over the course of one week at the CNIC, participants are introduced to the fundamentals of modern biomedical research. They gain hands-on experience by conducting supervised experiments, mastering advanced techniques, operating cutting-edge scientific equipment, and presenting their findings—all under the expert mentorship of CNIC researchers.

Fellowships in 2025: 8

Training for the CNIC Recognition Award Winner at the European Union Contest for Young Scientists

The CNIC Recognition Award was established in the 2022 edition of the European Union Contest for Young Scientists (EUCYS). The award offers a research stay at the CNIC for a student whose project aligns with the Center's research interests. The award is mentored by Dr. Mª Ángeles Moro, a long-standing member of the EUCYS selection committee.

The 2024 awardee, Ludmila Kvasnovska, from Slovakia, was recognized for her project "Potential Biomarkers of Age-Related Chronic Inflammation." She completed her CNIC internship in 2025, together with participants in the Acércate Program.

4º ESO – CNIC

The Madrid 4th Year ESO + Company Program, an initiative of the regional Directorate General of Secondary Education, aims to bridge the gap between the educational system and the labor market by offering educational placements in companies and institutions. This complementary activity program is being adopted by an evergrowing number of schools across the region, helping young people to make informed decisions about their academic and professional futures by motivating them and equipping them with essential skills.

The CNIC collaborates annually through the 4ºESO-CNIC Program. In 2025, 23 science students from 22 schools were selected from a pool of 125 applicants and spent three full days in the CNIC laboratories, exploring potential scientific careers.

PROGRAMS FOR UNDERGRADUATE STUDENTS

Internships are offered to university students in the following programs:

CICERONE PROGRAM

The Cicerone Program is open to advanced undergraduate students and Master's students in biomedicine-related disciplines. Participants extend their scientific training through hands-on experience of laboratory-based biomedical research during the summer recess. In addition to carrying out a supervised research project, the students attend CNIC seminars and workshops. The aim of the program is to give students first-hand knowledge of biomedical research so that they can make informed choices about pursuing a scientific career.

Fellowships in 2025: 31

CURRICULAR AND EXTRACURRICULAR UNIVERSITY PRACTICAL PROGRAM

The CNIC offers practical training in cardiovascular research to visiting undergraduate students through formal collaborative agreements with Spanish and international universities.

In 2025, 15 students from the following universities completed internships at the CNIC related to their final degree thesis dissertation (TFG) under the guidance of a CNIC supervisor:

8 students from the Autonomous University of Madrid
2 students from the Complutense University of Madrid
2 students from the University Alcalá de Henares
2 students from the University Carlos III of Madrid
1 student from the Polytechnic University of Madrid

In 2025, an additional 37 students from Spanish and international universities participated in various types of university internships at the CNIC under the mentorship of a CNIC supervisor. This group included 28 students from 10 Spanish universities, five Erasmus students from universities in Amsterdam, Naples, Pavia, Roma, and Twente, and four other international students from universities in Hamburg, Lyon, Toulouse, and Nanyang.

PROGRAMS FOR MASTER'S AND GRADUATE STUDENTS

MASTER'S FELLOWSHIP CNIC-ACCIONA PROGRAM AND FUNDACIÓN CAROLINA-CNIC MASTER'S FELLOWSHIP PROGRAM

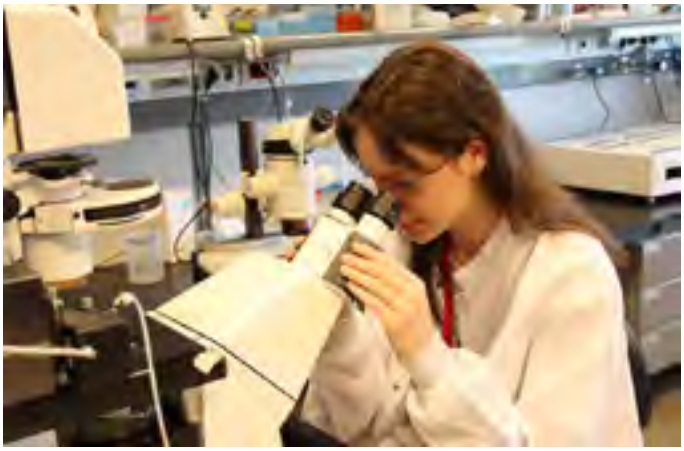
These grants provide funding for master's degree students enrolled at a Spanish university to carry out their experimental project (TFM) in a CNIC laboratory.

Fellowships in 2025: 9

Other Master's Student Internships

In 2025, another 18 students from the following universities worked on their TFM under the guidance of a CNIC supervisor:

7 students from the Autonomous University of Madrid
7 students from the Complutense University of Madrid
1 student from the University of Valencia
1 student from the University of Grenoble Alpes, France
1 student from the University of Amsterdam, the Netherlands
1 student from Maastricht University, the Netherlands



PREDOCTORAL (PhD) PROGRAM

The Predoctoral Program provides a unified framework for all CNIC researchers who are working toward a doctoral degree. All predoctoral researchers are signed up to this program, irrespective of their funding source.

The aims of the Program are to ensure uniform predoctoral training at the CNIC and further to ensure fair and equal access of predoctoral researchers to training opportunities.

The Program schedules regular meetings between the predoctoral fellow and his or her thesis committee, composed of the thesis director, another CNIC group leader, and an external expert.

Graduate students studying for a PhD degree at the CNIC in 2025: 93

Graduate students at the CNIC awarded a PhD degree in 2025: 14
Enrolled at the Autonomous University of Madrid: 11
Enrolled at the Complutense University of Madrid: 3

The CNIC PhD Office is the forum for scientific support, guidance, and growth of all PhD students enrolled on the CNIC Predoctoral Program, independently of their university affiliation or funding source. The office is coordinated by a group leader appointed by the CNIC management.

This office also includes two permanent members (Head of the CNIC Scientific Management office and a manager from the Research Office), and one senior and one junior PhD student, who are elected by the CNIC's PhD students.

FRONTIERS IN CARDIOVASCULAR RESEARCH MASTER'S MODULE

This postgraduate course is run by the CNIC as part of the **Universidad Autónoma de Madrid (UAM)** Molecular Biosciences Master's Program. This optional module provides a broad overview of cardiovascular biology, including perspectives from basic, clinical, and translational research.

Attendees on this course are enrolled UAM Master's students, CNIC predoctoral researchers, and participants in the Res@CNIC SEC Program (see below).

UAM Master's students in 2025: 14

PROGRAMS FOR RESIDENT MEDICAL INTERNS

RES@CNIC-SEC PROGRAM

The Res@CNIC-SEC Program, a collaboration with the **Spanish Society of Cardiology (SEC)**, offers resident medical interns the opportunity during the first years of their specialization period to learn about the latest techniques in cardiovascular research being used in the CNIC laboratories, under the guidance of a CNIC scientist. Residents on the program also receive training in theoretical aspects of cardiovascular research through an expert-led taught module. The program also seeks to create links and collaborations so that on conclusion of their MIR specialization period, these professionals will have the chance to undertake research projects in their respective hospitals in partnership with CNIC scientists.

Participants in 2025: 25 from the following hospitals:

- *Complejo Asistencial Universitario de León*
- *Hospital Universitario Fundación Jiménez Díaz*
- *Hospital Clínic de Barcelona*
- *Hospital Clínico San Carlos*
- *Hospital Universitario La Paz*
- *Hospital Universitario de Cruces*
- *Hospital Universitario de Navarra*
- *Hospital Universitario de Oviedo*
- *Hospital Universitario La Paz*
- *Hospital Universitario Lucus Augusti*
- *Hospital Universitario Puerta de Hierro*
- *Hospital Universitario Ramón y Cajal*
- *Hospital Universitario Virgen del Rocío*

INVESMIR CNIC-SEC PROGRAM

The INVESMIR SEC Program, a collaboration with the **Spanish Society of Cardiology (SEC)**, offers advanced resident medical interns the opportunity during their specialization period to extend their training through a research project in one of the CNIC's laboratories, under the supervision of a CNIC scientist.

An important aim of the program is for participants to establish contacts and collaborations with CNIC researchers that will support them, after completion of their MIR specialization training, in pursuing their own research projects at their centers within the Spanish National Health System. In 2025, two cardiology interns, from Hospital Universitario Joan XXIII (Tarragona) and Ciudad Real Hospital Complex, participated in the program.

MD-PHD CNIC-SEC PROGRAM

The new CNIC-SEC MD-PhD Program, also in collaboration with **the Spanish Society of Cardiology (SEC),** trains medical residents in advanced research in the fields of cardiology and cardiovascular disease. This program seeks to integrate clinical professional development with scientific research, so that participants can apply the knowledge they gain at their centers within the National Health System. The partnership between the CNIC and the SEC allows participants to conduct their doctoral thesis research in a world-class research environment with access to leading experts in the field.

Calls for the program are opened annually. Up to six positions will be awarded

OTHER EXTERNAL ROTATIONS

Seven residents from the following hospitals completed external rotations at the CNIC in 2025:

- *Hospital Universitario Príncipe de Asturias*
- *Hospital General Universitario de Ciudad Real*
- *Hospital Universitario Virgen de las Nieves*
- *Hospital Universitario Severo Ochoa*
- *Hospital Universitario Fundación Jiménez Díaz*

PROGRAMS FOR RESEARCHERS

CARDIO JOVEN CNIC-SEC PROGRAM

The aim of this program—another SEC collaboration—is to support high-quality translational cardiovascular research in the Spanish National Health System by providing theoretical and practical training to cardiologists with a research vocation. One trainee is selected every two years.

The program is aimed at cardiologists wanting to undertake advanced clinical and research at any center within the Spanish National Health System.

Specific aims:

a) To create the figure of the cardiologist researcher by providing high-quality training in clinical research methods, including statistical analysis and the latest basic research techniques used in cardiovascular biomedicine, as well as opportunities to explore any clinical area of cardiology in greater depth (sub-specialization.

b) International training visits toward a Master's Degree are offered at the London School of Hygiene and Tropical Medicine (90 ECTS).

COFUND CURE HEART AND BRAIN POSTDOCTORAL PROGRAM

The Cure Heart & Brain program collaborates with a diverse set of 24 partners to offer participating postdoctoral researchers secondment opportunities and specialized training.

The two calls of this program garnered a total of 67 applications, which were evaluated by members of the CNIC's External Scientific Advisory Committee. The selection and recruitment process adhered to the principles of the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers, ensuring a merit-based, independent, and transparent approach based on scientific excellence.

The program has enabled the recruitment of 12 international postdoctoral researchers (6 women and 6 men) from the Czech Republic, France, Germany, Italy, Portugal, the Netherlands, the United Kingdom, China, Cuba, Japan, and South Korea.

VALENTÍN FUSTER PROGRAM

The VALENTÍN FUSTER Program was created to train a new generation of translational cardiovascular researchers—clinicians and scientists who can connect research and patient care, applying scientific advances in the clinic while using real-world clinical challenges to drive new research.

At the same time, the program promotes the integration of research as a fundamental part of the medical career within the Spanish National Health System.

This program—a partnership with the 12 de Octubre Hospital Research Institute (i+12)—supports the appointment of a physician specializing in translational cardiovascular research at 12 de Octubre University Hospital (H120) through a five-year contract.

PRACTICAL TRAINING FOR TECHNICAL SCHOOL STUDENTS

In 2025, the program welcomed nine technical school students for three-month placements in CNIC laboratories. Participants were enrolled in vocational programs in Pathological Anatomy and Cytodiagnostics, Clinical and Biomedical Laboratory, and Cell Culture, gaining hands-on experience in a research environment.

CNIC supports these placements through collaboration agreements with 21 technical training colleges. Each college nominates one candidate, and host research groups select participants from the submitted applications.

The CNIC also works with two public centers in Madrid that offer intensive biomedicine-related training: Instituto de Educación Secundaria Moratalaz, which specializes in Clinical and Biomedical Laboratory, and Instituto de Educación Secundaria San Juan de la Cruz, which focuses on Diagnostic Imaging and Nuclear Medicine. In September 2025, seven students from these centers began extended seven-month placements at the CNIC.

CNIC CONTINUING EDUCATION PROGRAM

CARDIOVASCULAR PATHOPHYSIOLOGY COURSE: FROM SYMPTOMS TO GENES

This course is organized by the CNIC in partnership with the SEC. The course is aimed at R3, R4, and R5 residents in cardiology and other specialties related to cardiovascular disease, as well as translational researchers working in the field of cardiology.

Participants are given an overview of the molecular and genetic factors underlying cardiac diseases and gain a current understanding of cardiac physiology through the presentation and discussion of papers authored by CNIC scientists. These sessions are further enriched by contributions from a clinical expert specializing in the topic of each paper.

The 2025, XVII edition of this course, was held online in the SEC Campus and was attended by 149 participants.

6 FACTS AND FIGURES

Back to Contents

SCIENTIFIC PUBLICATIONS 2025

PUBLICATIONS IN WoS IN JOURNALS WITH AN IMPACT FACTOR

	NUMBER	PERCENTAGE
Articles	260	64.5 %
Reviews	31	7.7 %
Other	112	27.8 %
Total	403	

a)

JOURNAL'S QUALITY	NUMBER	PERCENTAGE
D1	232	57.6%
Q1	356	88.3%
Q2	36	8.9%
Q3	9	3.3 %
Q4	2	0.5 %

b)

OPEN ACCESS	NUMBER	PERCENTAGE
All types of OPEN ACCESS	403	100%
GOLD OPEN ACCESS	261	64.8 %

c)

LEADERSHIP	NUMBER	PERCENTAGE
First, last or corresponding author	195	48.4 %

d)

COLLABORATIONS	NUMBER	PERCENTAGE
International collaboration	280	69.5 %
National collaboration	113	28.0 %
Only CNIC authors	10	2.5 %

e)

OTHER IMPACT INDICATORS	NUMBER	PERCENTAGE
Docs Cited	211	52.4 %
Highly cited papers*	24	6.0 %
Hot Papers**	4	1.0 %

TOP 3 : PUBLICATIONS IN THE TOP THREE JOURNALS WITHIN THEIR CATEGORIES

100 25%

THE LANCET

The NEW ENGLAND JOURNAL of MEDICINE

nature

Science

nature reviews cardiol

Circulation

European Heart Journal

JOURNAL OF HEPATOLOGY

EUROPEAN RESPIRATORY journal

Respiratory and Critical Care Medicine

Circulation Research

JACC Cardiovascular Imaging

Science Translational Medicine

Filter Summary:

Dataset: Web of Science (WoS)

Domestic/International Collaboration: All

Time Period: [2025, 2025]

Include Early Access documents: true

Document Type: [All types of documents]

Organization Name: [Centro Nacional de Investigaciones Cardiovasculares (CNIC)]

Exported date: 13/03/2026

*Highly Cited Papers: Articles that have received enough citations to be ranked in the top 1% in their respective scientific areas, type of document and year of publication.

**Hot Papers: Articles that in the export date have received enough citations to be positioned in the top 0.1% in the respective scientific areas, type of document and year of publication.

List of all CNIC 2025 Publications at

https://www.cnic.es/es/investigacion/publicaciones/resultados?y=2025

COMPETITIVE FUNDING*

Back to Contents

Grants starting 2025

NATIONAL	INTERNATIONAL
44 grants	13 grants
€ 6.296.921	€ 7,357,618

Grants active in 2025

NATIONAL	INTERNATIONAL
234 grants	48 grants
€ 54.097.729	€ 35,223,902

Highlighted projects:

Ministerio de Ciencia, Innovación y Universidades

1 Severo Ochoa Centre of Excellence grant
4 Public-Private Partnership projects
5 Scientific and Technical Equipment projects

Other National Funding Sources

3 Personalised Medicine Partnership projects_ISCIII
6 Research Group projects_Community of Madrid
6 Spanish Society of Cardiology projects
6 Spanish Association Against Cancer projects
12 Health Research projects la Caixa Foundation

Highlighted projects:

European Union-funded

1 Future and Emerging Technologies project
1 Innovative Health Initiative project
1 EU4Health Joint Action
2 European Innovation Council projects
3 Marie Skłodowska-Curie Actions projects
5 Collaborative Health networks H2020&HE
7 ERA4Health European Partnership projects
10 European Research Council projects

Other International Funding Sources

1 Novo Nordisk project
1 Worldwide Cancer Research project
1 British Heart Foundation project
1 Bright Focus Foundation project
2 U.S. National Institutes of Health networks
3 Leducq Foundation projects

TECHNOLOGY TRANSFER*

Active Patent families	22
Active patents	198
New patent families	6
New patent applications	12
Licensed inventions	10
Active Research Collaboration Agreements (RCAs)	6
New Confidential Disclosure Agreements (CDAs)	11
New Material Transfer Agreements (MTAs)	53

*Data as of 31/12/2025

HUMAN RESOURCES*

Back to Contents

Scientific and Technical Staff

416

Women 254

Men 162

From outside Spain 52 (13%)

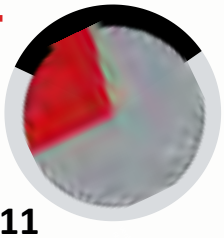
20 countries

Group Leaders

32

Women 9

Men 23



Cardiologists 11

Heads of Technical Units

10

Women 5

Men 5

Visiting Scientists

217

Women 125

Men 92

From institutions outside Spain 33 (15%)

13 countries

*Data as of 31/12/2025

CONTENTS

Back to Contents

SCIENTIFIC ADVISORY BOARD*

Back to Contents

PRESIDENT

Karin R. Sipido
Division of Experimental Cardiology
Katholieke Universiteit Leuven, Belgium

SECRETARY

Pedro Luis Sánchez
University Health Care Complex of Salamanca and
University of Salamanca, Spain

MEMBERS

Chiara Bucciarelli-Ducci
Royal Brompton and Harefield NHS Foundation
Trust and King's College, London, UK

Anna Dominiczak
Institute of Cardiovascular and Medical Sciences,
University of Glasgow, UK

Mauro Giacca
School of Cardiovascular Medicine & Sciences
King's College London, UK

Hélène Girouard
University of Montreal, Canada

Gerd Heusch
Institute of Pathophysiology, Center of Internal
Medicine. University of Essen Medical School,
Germany

Esther Lutgens
Mayo Clinic, Rochester, USA

Ajay M. Shah
Kings College London, London, UK

Filip Swirski
Icahn School of Medicine at Mount Sinai
New York, USA

*Data as of 31/12/2025

PUBLIC AND PRIVATE COMPETITIVE GRANT-AWARDING BODIES

Back to Contents

- AFM TELETHON
- AGENCIA ESTATAL DE INVESTIGACIÓN
- ASTRAZENECA FARMACÉEUTICA ESPAÑA
- BOEHRINGER INGELHEIM GMBH
- BRITISH HEART FOUNDATION
- COMUNIDAD DE MADRID
- EUROPEAN COMMISSION
- EUROPEAN RESEARCH COUNCIL
- EUROPEAN FOUNDATION FOR THE STUDY OF DIABETES (EFSD)
- EUROPEAN MOLECULAR BIOLOGY ORGANIZATION
- FUNDACIÓN CIENTÍFICA DE LA AECC
- FUNDACIÓN EUGENIO RODRÍGUEZ PASCUAL
- FUNDACIÓN INOCENTE INOCENTE
- FUNDACIÓN ISABEL GEMIO
- FUNDACIÓN LA CAIXA
- FUNDACIÓN LA MARATÓ TV3
- FUNDACIÓN RAMÓN ARECES
- IBSA FOUNDATION
- INSTITUTO DE SALUD CARLOS III
- LEDUCQ FOUNDATION
- MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES
- MINISTERIO DE EDUCACIÓN, CULTURA Y DEPORTE
- MINISTERIO DE TRABAJO Y ECONOMÍA SOCIAL
- MINISTERIO DE TRANSFORMACIÓN DIGITAL Y FUNCIÓN PÚBLICA
- NATIONAL INSTITUTES OF HEALTH
- NOVONORDISK
- SOCIEDAD ESPAÑOLA DE CARDIOLOGÍA
- SOCIEDAD ESPAÑOLA DE GENÉTICA
- WORLDWIDE CANCER RESEARCH

CENTRO NACIONAL DE INVESTIGACIONES CARDIOVASCULARES CARLOS III (F.S.P.)
Melchor Fernández Almagro, 3
28029 - Madrid (Spain)
Tel.: (+34) 914531200
www.cnic.es