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SCIENTIFIC REPORT 2024

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MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES
Instituto de Salud Carlos III
Fundación pro cnic
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EXCELENCIA SEVERO OCHOA 2022-2025
AGENCIA ESTATAL DE INVESTIGACIÓN

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.

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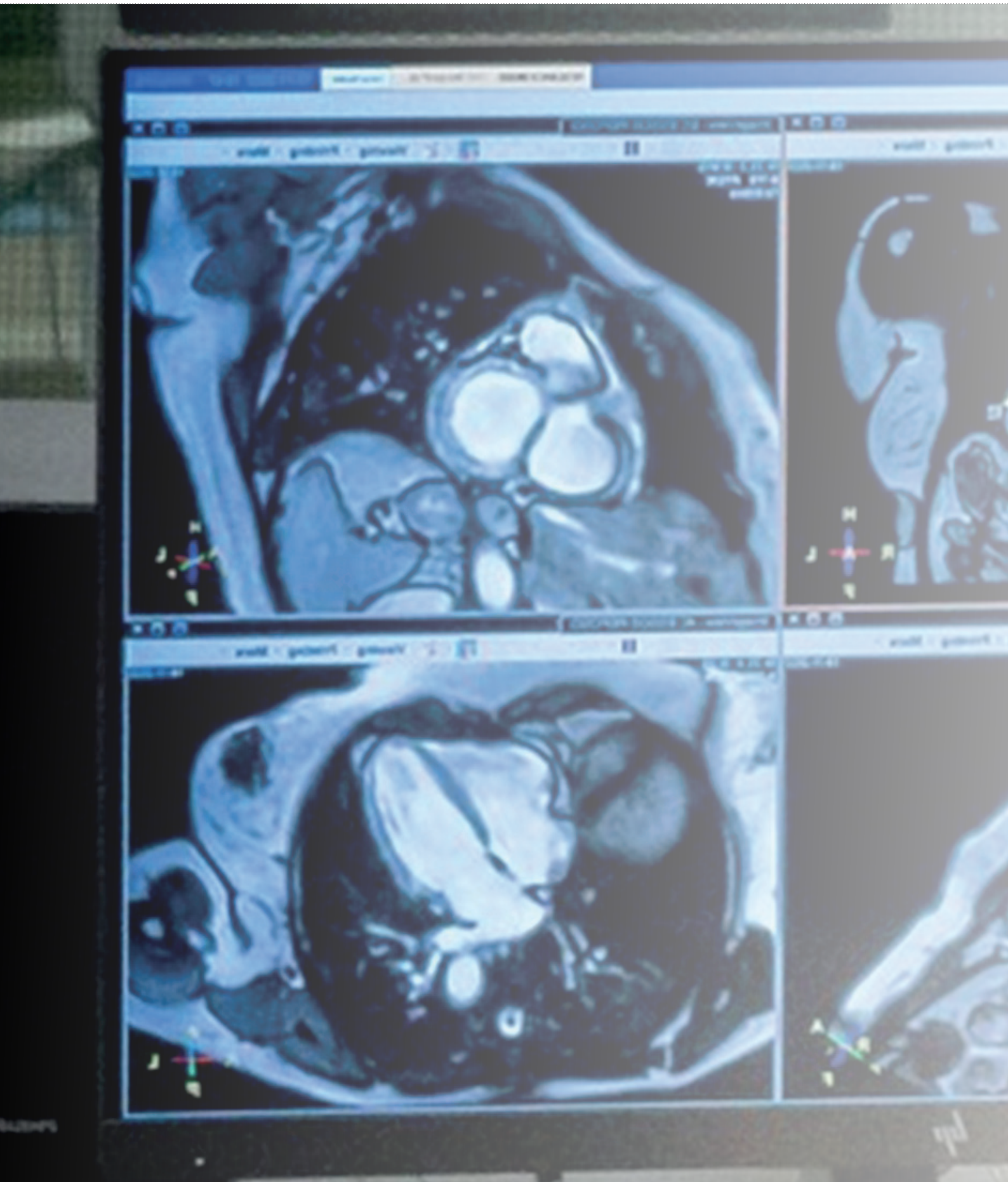


CONTENTS

1 FOREWORD AND CNIC MISSION

Valentín Fuster, General Director

Borja Ibáñez, Scientific Director and Clinical Research Director

Vicente Andrés, Basic Research Director

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 programmatic performance.

Cardiovascular disease (CVD) remains the leading cause of death worldwide. The escalating costs of managing CVD in its symptomatic stages place a growing burden on patients, families, and healthcare systems. In response, the CNIC has defined three overarching goals: to advance understanding of cardiovascular health, improve disease prevention and health promotion, and drive therapeutic innovation for prevalent forms of CVD. Achieving these goals requires mechanistic studies to uncover the molecular and cellular basis of disease, alongside clinical research to translate discoveries into improved strategies for health promotion, diagnosis, and care.

To meet these challenges, the CNIC operates on four pillars: excellence in basic and clinical research, advanced technology, collaborative networking, and training. Scientific activity is structured across two interlinked departments—Basic Research and Clinical Research—and seven integrated research programs: (1) novel mechanisms of atherosclerosis; (2) myocardial homeostasis and cardiac injury; (3) cardiovascular regeneration; (4) novel arrhythmogenic mechanisms; (5) cardiovascular risk factors and brain health; (6) cardiovascular health promotion; and (7) technology development. These programs span the full translational spectrum—from discovery science to large-scale clinical trials—and leverage the CNIC's strengths in cutting-edge technologies, animal and cellular models, imaging, and data science.

In 2024, CNIC welcomed two new Group Leaders: Dr. Fátima Sánchez Cabo (Computational Systems Biomedicine) within the atherosclerosis program, and Dr. Ana Devesa (Cardiometabolic Disease and Advanced Imaging) within the myocardial homeostasis program.

The CNIC's research has directly shaped clinical practice: six of its major studies (SECURE, PESA, TAN-SNIP, FOCUS, AWHS, and Reboot) contributed twelve key recommendations to the European Society of Cardiology's 2024 clinical guidelines in hypertension, acute coronary syndromes, and peripheral and aortic arterial disease. As of 2024, the CNIC leads 23 clinical studies and trials involving 14,883 adults and 50,000 children.

A major highlight of 2024 was the launch of REACT, an ambitious international precision medicine initiative co-led by CNIC and Denmark's Rigshospitalet and funded by the Novo Nordisk Foundation. Building on insights from the PESA CNIC-Santander study, REACT will analyze 16,000 individuals (8,000 in Spain) to advance personalized atherosclerosis prevention. The study is designed in two phases over eight years, with €23 million secured for the first 2.5-year phase. Through REACT, CNIC is driving a new era in cardiovascular prevention and reinforcing its leadership in translational research.

In 2024, the CNIC secured €3.5 million through two national Artificial Intelligence R&D excellence projects awarded by the Ministry for Digital Transformation and Public Administration. It also received €3.9 million in funding from RED.ES for the CardiotrAIning initiative, supporting 15 contracts to promote AI and Big Data training in cardiovascular health. An additional €2 million was awarded by the Ministry of Science, Innovation and Universities for scientific equipment acquisition.

Internationally, the CNIC participated in 18 consortia funded through Horizon 2020 and Horizon Europe, coordinating six. The center also contributed to five ERA4Health CARDINNOV initiatives and maintained active collaborations with major global organizations including the Leducq Foundation, NIH, and British Heart Foundation.

Another key milestone was CNIC's role in the EU4HEALTH Joint Action JACARDI, a €53 million initiative spanning 21 European countries to address major public health challenges.

Further, CNIC received €1.7 million from the European Commission for the MSCA COFUND program Cure Heart and Brain, implemented in collaboration with 24 international partners. In 2024, the program supported the incorporation of three postdoctoral researchers, with nine more to follow in 2025.

The CNIC's most impactful innovation to date is the cardiovascular polypill, developed in collaboration with Ferrer laboratories. This once-daily medication for post-myocardial infarction patients—now included in the WHO List of Essential Medicines and marketed in 29 countries—has been shown to reduce cardiovascular events by 24% and cardiovascular mortality by 33%. The polypill exemplifies CNIC's commitment to research with direct patient benefit.

Further achievements from 2024 are detailed throughout this report. As we look ahead, CNIC remains committed to excellence, innovation, and collaboration across disciplines. By integrating basic and clinical research, the center will continue to generate impactful discoveries and train the next generation of scientists working to reduce the global burden of cardiovascular disease.

2 RESEARCH AT THE CENTER

2.1 SCIENTIFIC PROGRAMS

The CNIC is organized into two departments, one focused on Basic Research and the other on Clinical Research. Research in these fields is fully interconnected through seven focused Programs.

2.1.1 NOVEL MECHANISMS OF ATHEROSCLEROSIS

Coordinator: **José Javier Fuster**

Clinical Leaders: **Valentín Fuster and Inés García Lunar**

The **Novel Mechanisms of Atherosclerosis Program** aims to advance our understanding of the pathophysiology of atherosclerosis, the main cause of cardiovascular and cerebrovascular diseases. Despite effective interventions targeting traditional risk factors, a significant residual risk of atherosclerotic cardiovascular disease persists, even in individuals with well-controlled cholesterol levels and low estimated cardiovascular risk. This highlights the need to explore non-conventional risk factors and underlying disease mechanisms to develop novel strategies for the prediction, prevention, and treatment.

The program brings together multidisciplinary teams that integrate experimental research in animal models and human studies, leveraging data from the Progression of Early Subclinical Atherosclerosis [PESA] cohort and other populations. Research efforts are focused on two main areas:

Inflammatory Mechanisms of Atherosclerosis: Atherosclerosis is firmly established as an inflammatory disease driven by maladaptive immune responses to chronic cardiovascular risk factor exposure. However, translating inflammation-targeted therapies into clinical practice remains challenging, underscoring the need for a deeper understanding of the complex inflammatory pathways involved.

Additional Key Mechanisms: Other research groups explore vascular cell biology, mechanosensing in the vascular wall, microbiota-derived metabolites, and the identification of circulating and imaging biomarkers to improve risk assessment and early atherosclerosis detection.

KEY ACHIEVEMENTS IN 2024

Clonal Hematopoiesis and Atherosclerosis

Program scientists uncovered critical links between atherosclerosis and acquired mutations driving clonal hematopoiesis—an emerging cardiovascular risk factor. This work also identified the anti-inflammatory drug colchicine as a promising personalized preventive strategy for individuals carrying specific mutations (Nature Medicine 2024; European Heart Journal 2024).

Endothelial Dysfunction in Hutchinson-Gilford Progeria Syndrome

Program researchers elucidated the molecular and cellular mechanisms linking endothelial dysfunction to accelerated atherosclerosis in Hutchinson-Gilford progeria syndrome, a rare genetic disorder characterized by premature aging and early death, primarily due to atherosclerosis-related complications (Circulation 2024; Journal of Clinical Investigation 2024).

Subclinical Atherosclerosis and Mortality Risk

Findings from the BioImage US cohort revealed that noninvasive imaging, particularly vascular ultrasound, significantly predicts all-cause mortality risk beyond traditional risk factors. Atherosclerosis progression over time also emerged as an independent predictor of mortality (Journal of the American College of Cardiology 2024).

Macrophage Imaging in Cardiovascular Disease

A study on macrophage imaging via positron emission tomography in mouse models of cardiovascular disease was recognized as Paper of the Year 2024 by npj Imaging.

Additional High-Impact Publications

Additional research was published in leading journals in 2024, including Nature Cardiovascular Research, Nature Communications, and Proceedings of the National Academy of Sciences.

OUTREACH AND ENGAGEMENT

The Program remains committed to sharing knowledge and engaging with the scientific community and the public. In 2024, program researchers presented their findings at prestigious international conferences, including:

The European Society of Cardiology annual congress

The European Hematology Association annual congress

The 2nd International Conference on Mesenchymal Cells in Health and Disease

The 29th Krakow Conference on Endothelium

In addition to contributing to these global forums, Program scientists played a key role in organizing the CNIC Conference: Understanding Immunity in Cardiovascular Disease, which convened leading national and international experts to discuss advances in cardiovascular immunology and immunotherapy.

The Program also emphasized public outreach, participating in events designed to make cardiovascular research accessible to a broader audience. Highlights included:

Participation in the ***Bringing Researchers Into the Light*** event, held at CaixaForum Madrid during European Researchers' Night 2024.

Leading the ***Mini-Cardioguía Infantil y Juvenil***, an interactive event hosted at the CNIC as part of the Madrid Science and Innovation Week, reaching over 100 children and adults.

RESEARCH GROUPS

Vicente Andrés
Molecular and Genetic Cardiovascular Pathophysiology

Jacob Fog Bentzon
Experimental Pathology of Atherosclerosis

Miguel Angel 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

David Sancho
Immunobiology

Jesús Vázquez
Cardiovascular Proteomics

These efforts foster awareness and dialogue on cardiovascular health, inspiring the next generation of researchers and clinicians.

HIGHLIGHTED PUBLICATIONS

Circulation. 2024 150(20):1612-1630. doi:10.1161/CIRCULATIONAHA.

European Heart Journal. 2024 45(43):4601-4615. doi:10.1093/eurheartj/ehae546.

Journal of Clinical Investigation. 2024 134(22):e173448. doi:10.1172/JCI173448.

Journal of the American College of Cardiology. 2024 84(15):1391-1403. doi:10.1016/j.jacc.2024.06.045.

Nature Cardiovascular Research. 2024 3(2):203-220. doi:10.1038/s44161-023-00412-w.

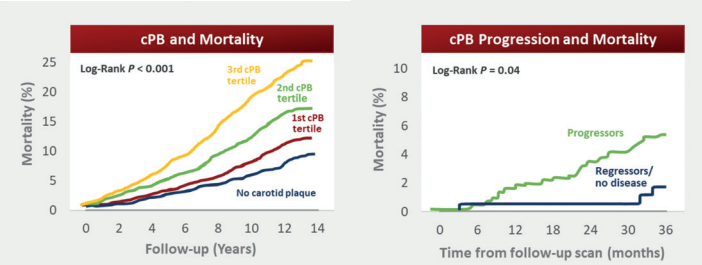
Nature Communications. 2024 15(1):10102. doi:10.1038/s41467-024-54224-y.

Nature Medicine. 2024 30(10):2857-2866. doi:10.1038/s41591-024-03213-1.

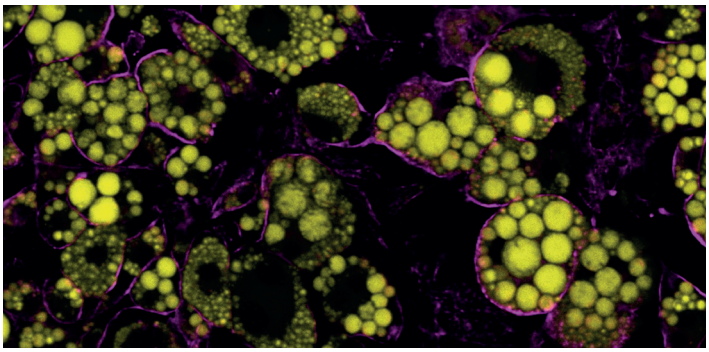
npj Imaging. 2024 2(1):12. doi:10.1038/s44303-024-00009-3.

Proceedings of the National Academy of Sciences. 2024 121(18):e2400752121. doi:10.1073/pnas.2400752121.

Nature Medicine cover (Vol. 30, No.10, 2024). Researchers in the Program found that clonal hematopoiesis confers an increased risk of atherosclerosis development, whereas atherosclerosis does not affect the risk of clonal hematopoiesis, indicating a unidirectional connection between these conditions (*Díez-Díez et al, Nature Medicine 2024, 30:2857-866*). *Image: Rosa Moro, CNIC*.



Influence of subclinical atherosclerosis burden and progression on mortality. The Bioimage study enrolled 5,716 asymptomatic individuals who underwent non-invasive imaging assessment to assess subclinical atherosclerosis. Carotid plaque burden (cPB) was quantified, and cardiovascular risk factors were evaluated. A subset of 732 participants underwent a second assessment after a median follow-up of 8.9 years. All participants were followed for all-cause mortality. Higher atherosclerosis burden at baseline, and more importantly, cPB progression over time, were significantly associated with mortality, independently of conventional cardiovascular risk factors and medication. *Modified by Rosa Moro (CNIC) from Fuster V et al JACC. 2024, 84:1391–1403*.



Confocal microscopy imaging of cultured adipocytes (fat cells) containing fat droplets (yellow) and the caveolin 1 protein in the cell membrane (magenta). Scale bar, 100 microns. Researchers in the Program found that genetically modified adipocytes expressing a non-phosphorylatable form of caveolin 1 accumulate caveolae, because they are unable to flatten in response to fat accumulation. Mutations in this protein are associated with human lipodystrophy. *Aboy-Pardal et al. Nature Communications 2024, 15:10102*.

2.1.2 MYOCARDIAL HOMEOSTASIS AND CARDIAC INJURY (MERCURY)

Coordinator: **Enrique Lara-Pezzi**
Clinical Leader: **Borja Ibáñez**

The **MERCURY research program** focuses on uncovering the pathomechanisms of heart diseases to develop new therapeutic strategies, with activities organized around two main focus areas:

- The mechanisms underlying the cardiotoxic effects of anti-tumor treatments
- The genetic and molecular causes of inherited cardiomyopathies

KEY ACHIEVEMENTS IN 2024

MERCURY program scientists made significant strides last year in all these areas, contributing to our overarching goal of developing targeted treatments to effectively prevent and manage heart disease.

Cardiotoxicity Induced by Anti-Tumor Treatments

Research on cardiac atrophy associated with anthracycline treatment has revealed that a high-protein diet before, during, and after doxorubicin administration mitigates cardiac atrophy. Preliminary proteomics data suggest this effect is linked to sarcomeric modifications. Current studies are analyzing sarcomeric protein phosphorylation, conformational changes in cardiac myosin (using the Mant-ATP assay), genetic mechanisms, and titin cleavage to better understand the structural and functional changes caused by anthracycline treatment.

Using engineered mouse models, we have found that individuals carrying gene variants associated with hypertrophic cardiomyopathy may also face a higher risk of fatal chemotherapy-induced cardiotoxicity. Clinical validation of these findings is ongoing. Additionally, we have uncovered a novel role of the giant protein titin in mediating pathogenic remodeling in both skeletal and cardiac muscle. This discovery opens new opportunities for developing drugs to prevent damaging remodeling processes in musculoskeletal and cardiac diseases.

In a large animal model of anthracycline-induced cardiotoxicity in pigs, chronic treatment with the sodium-glucose co-transporter 2 (SGLT2) inhibitor empagliflozin completely prevented cardiotoxicity. Our findings suggest that empagliflozin shifts cardiac metabolism toward increased ketone body utilization, offering a potential cardioprotective mechanism. These results highlight the therapeutic potential of SGLT2 inhibitors in preventing chemotherapy-induced heart damage.

Genetic and Molecular Causes of Inherited Cardiomyopathies

Dilated Cardiomyopathy (DCM)

Our research has advanced the understanding of the genetic basis of DCM by analyzing the rate at which genetic carriers develop the disease and identifying risk factors associated with its progression. These findings have laid the groundwork for the **EarlyGene trial**, coordinated by the CNIC. This trial integrates genetic screening with advanced imaging techniques to evaluate whether early treatment of genetic carriers can modify the natural progression of DCM, potentially enabling preventive interventions in at-risk populations.

Arrhythmogenic Cardiomyopathy (ACM)

We have developed innovative treatments for ACM, a condition often caused by genetic mutations. Our studies identified SGK1 as a critical regulator of QRS complex prolongation in a PKP2 CT-mutant ACM mouse model. SGK1 activation leads to Cx43 hyperphosphorylation and lateralization, disrupting gap junctions and worsening conduction defects. Uing AAV-driven SGK1 activation, we replicated these abnormalities, confirming SGK1's pathogenic role. Importantly, both genetic and pharmacological inhibition of SGK1 restored proper Cx43 localization and significantly reduced QRS prolongation, suggesting that SGK1 inhibition could be a promising therapeutic approach for ACM.

We have also developed a novel therapy for the aggressive ACM caused by the S358L mutation in TMEM43. Building on a mouse model that faithfully replicates the human disease, we generated gene therapy tools to overexpress the wild-type TMEM43 protein. This approach significantly improved cardiac function, highlighting the potential of gene therapy for TMEM43-related ACM.

Right Ventricular Dysfunction

Research by MERCURY program scientists has identified metabolic changes critical to right-ventricular dysfunction under pressure overload conditions. These findings may lead to new opportunities for prevention and treatment.

HIGHLIGHTED PUBLICATIONS

JACC CardioOncol 6:217-232 (2024). doi: 10.1016/j.jaccao.2024.02.005

J Am Coll Cardiol 83:1640-1651 (2024). doi: 10.1016/j.jacc.2024.02.036.

Basic Res Cardiol Jun;119(3):419-433 (2024). doi: 10.1007/s00395-024-01041-5.

OUTREACH

"DNA-Adventure: explore DNA and edit!". European Researchers' Night, CNIC, 2024.

"DNA-Adventure: DNA extraction workshop". Science and Innovation Week, CNIC, 2024.

Interactive workshops for children. Science and Innovation Week, CEIP Rabindranath Tagore, Madrid, 2024.

RESEARCH GROUPS

Jorge Alegre-Cebollada
Molecular Mechanics of the Cardiovascular System

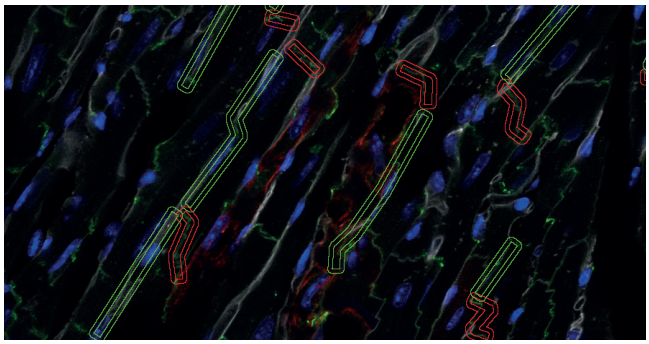
Ana Devesa
Cardiometabolic Disease and Advanced Imaging

Ana García Álvarez
Heart Failure and Pulmonary Hypertension Translational Research

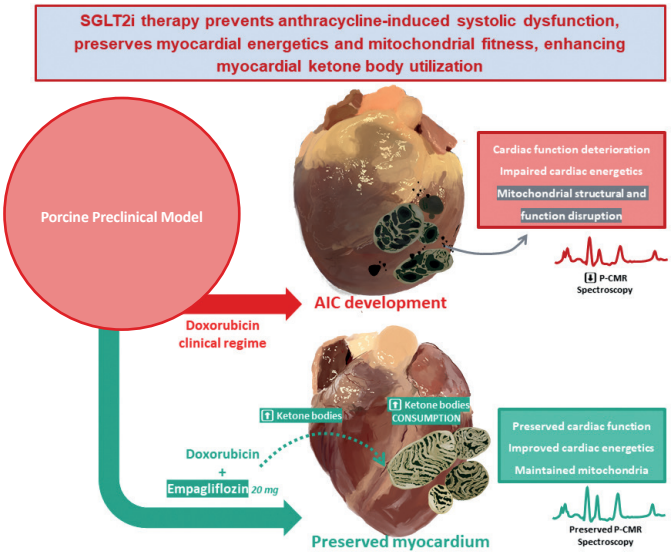
Pablo García-Pavía
Inherited Cardiomyopathies

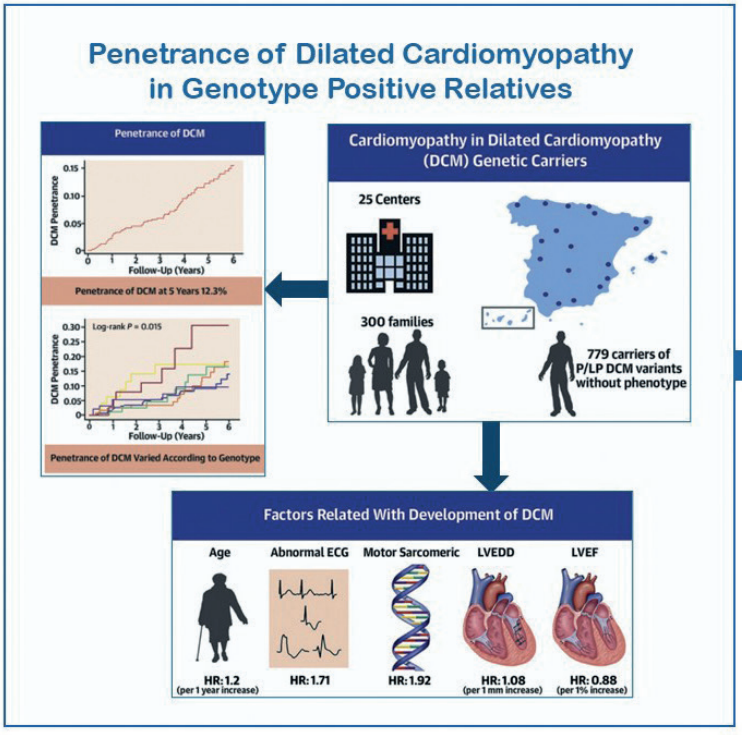
Borja Ibáñez
Translational Laboratory for Cardiovascular Imaging and Therapy

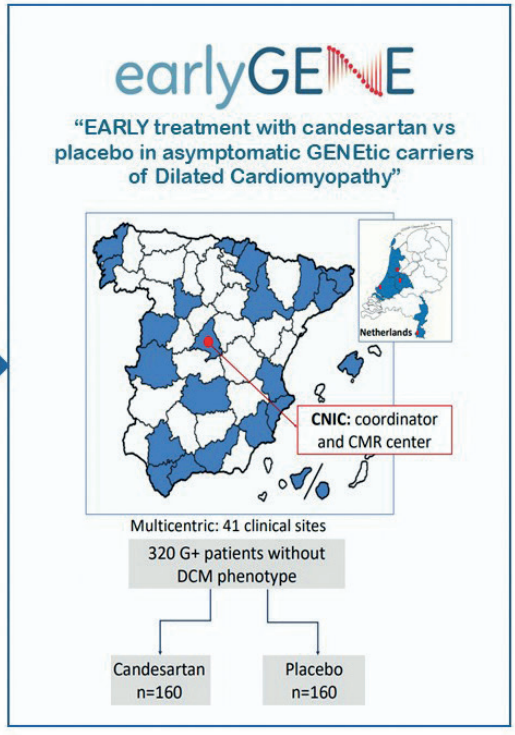
Enrique Lara-Pezzi
Molecular Regulation of Heart Failure



Histological section of murine myocardium. Red and green geometrical shapes are used to quantify subcellular location of proteins involved in the electromechanical coupling of cardiomyocytes, which is affected during myocardial disease







2.1.3 CARDIOVASCULAR REGENERATION

Coordinador: **Miguel Torres**
Clinical Leader: **Hesham Sadek**

The **Cardiovascular Regeneration Program (CVRP)** aims to understand the fundamental principles of heart and vasculature development and regeneration, using this knowledge to develop new therapeutic strategies for cardiovascular diseases. A key focus of the program is the metabolic regulation of cardiac regenerative ability. In 2024, the CVRP made significant progress, uncovering new targets and therapeutic approaches.

KEY ACHIEVEMENTS IN 2024

Metabolic Regulation of Cardiac Regeneration

Mitochondrial Complex I Discovery: Jose Antonio Enríquez's group identified an unsuspected role for mitochondrial complex I, revealing that the long-sought sodium channel in the mitochondrial inner membrane is embedded within complex I. This paradigm-shifting discovery changes our understanding of how the mitochondrial membrane protential is built and has important implications for its modulation (Cell, 2024).

Cox7a1-Deficient Zebrafish: Nadia Mercader and Jose Antonio Enríquez's groups joined forces to study Cox7a1-deficient zebrafish, demonstrating the critical role of *Cox7a1* in striated muscle homeostasis. Interestingly, the *Cox7a1*-deficient fish exhibited improved cardiac regeneration capacity, highlighting the importance of the modulation of super-complex their formation for the control of cardiomyocyte proliferation, as well as identifying a potential target for pro-regenerative strategies (Developmental Cell, 2024).

Cardiomyocyte Proliferation and Regeneration

FDA-Approved Drugs for Regeneration: Hesham Sadek and colleagues developed a virtual drug screening approach to identify compounds that disrupt the transcriptional activity of the Meis1/Hoxb13 heterodimer, a known barrier to cardiac regeneration. The team identified two aminoglycoside antibiotics capable of inhibiting Meis1/Hoxb13 activity and promoting cardiomyocyte proliferation and heart regeneration in mice and pigs. These drugs are already approved for human use in other settings, and the findings are poised to move to clinical trials (Nature Cardiovascular Research, 2024a).

Mechanistic Studies in Heart Disease and Development

Single-Cell Resolution Tools: Rui Benedito's group developed advanced tools in mouse models, enabling precise genetic dissection of molecular pathways at singe-cell resolution in vivo (Nucleic Acids Res, 2024; Nature Methods, 2024).

Bicuspid Aortic Valve Genetics: Jose luis de la Pompa's group uncovered new genetic determinants of bicuspid aortic valve and began characterizing genes involved in ventricular wall maturation and cardiomyopathy (Disease Models and Mechanisms, 2024).

Cell Competition in Cardiomyocytes: Miguel Torres and colleagues identified regulatory elements in the *Myc* gene responsible for cell competition, a mechanism that enables the replacement of cardiomyocyte populations in the adult heart (Nature Communications, 2024).

Cardiomyocyte Electrical Activity and Disease

Models of Rare Genetic Cardiac Disorders: Dr José Jalife and colleagues developed new mouse models that provide mechanistic insights into Andersen-Tawil Syndrome (Circulation Res, 2024) and Type-III Short-QT Syndrome(Cardiovascular Research, 2024a).

Meis Transcription Factors: Miguel Torres' group described the first models of Meis transcription factor deficiency in the cardiac conduction system, demonstrating the essential role of Meis proteins in pacemaker activity and atrioventricular conduction (Cardiovascular Research, 2024b).

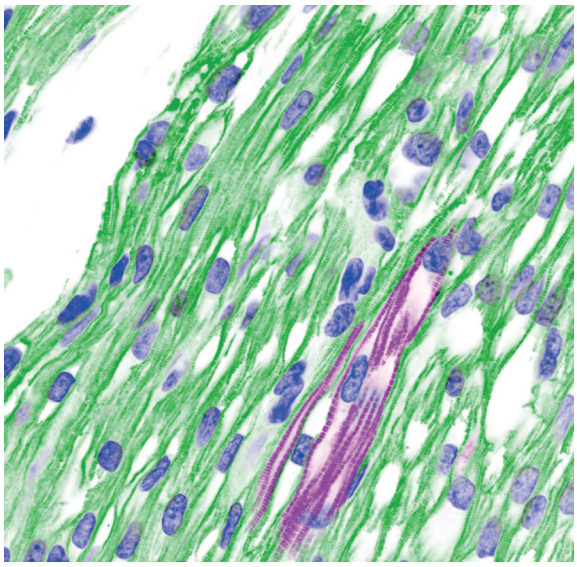
IPSC-Derived Cardiomyocytes: Florian Weinberger's team established IPSC-derived cardiomyocyte studies at the CNIC, showing that these cells can promote electrical impulse initiation and propagation when transplanted to infarcted rodent hearts (Stem Cell Reports, 2024). Weinberger also published a comprehensive review IPSC-derived cardiomyocyte transplantation strategies (Nature Cardiovascular Research, 2024b).

HIGHLIGHTED GRANTS IN 2024

Leducq Transatlantic network: Jose Luis de la Pompa secured $1.12 million for the **PlacHeart Network**, focusing on the placenta's role in maternal and fetal cardiovascular health and disease (January 2025-December 2030).

La Caixa Research Grant: Hesham Sadek received funding for research into **a new therapeutic strategy to combat heart disease**.

Advanced ERC Grant. Miguel Torres was awarded €2.5 million for the REACTIVA project, investigating the transcriptional regulation of cardiomyocyte polyploidization and its relevance in cardiac regeneration (October 2024–September 2029).



Engrafted human induced pluripotent stem cell-derived cardiomyocytes expressing the atrial (pink) or ventricular (green) myosin-light chain isoform respectively.

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 (GENOXPHOS)

Andrés Hidalgo
Imaging the Cardiovascular Inflammation and the Immune Response

José Jalife
Cardiac Arrhythmia

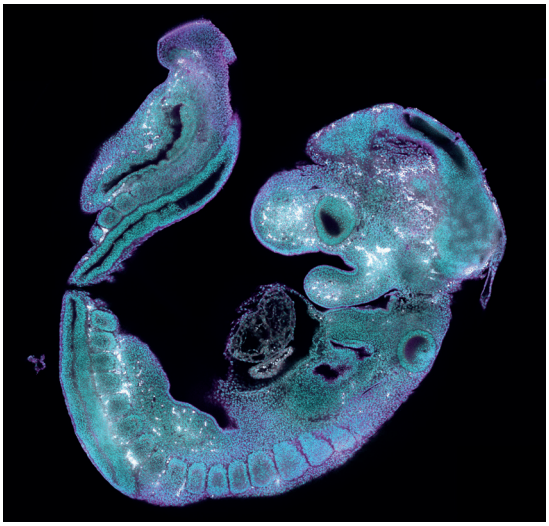
Nadia Mercader
Development of the Epicardium and its Role during Regeneration

Hesham Sadek
Myocardial Regeneration Vía Cardiomyocyte Cell Cycle Regulation

Miguel Torres
Genetic Control of Organ Development and Regeneration

Florian Weinberger
Cardiac Tissue Engineering and Regenerative Therapies

Pluripotent Cells in Action. The image shows an optical section of the gastrulating mouse embryo showing very active proliferative activity (green) of the naturally occurring pluripotent cells. Cell membranes appear in pink.



Myc expression in the mammalian embryo. A saggital section of the 9-day mouse embryo reveals the expression of Myc, one of the pluripotency reprogramming factors (pink), in stem cells of different organs.

HIGHLIGHTED PUBLICATIONS

Cardiovascular Research. 2024a 120:490-505. doi: 10.1093/cvr/cvae019

Cardiovascular Research. 2024b cvae258, doi:10.1093/cvr/cvae258

Cell. 2024 187:6599-6613.e21. doi: 10.1016/j.cell.2024.08.045

Circulation Research. 2024 134:e52-e71. doi: 10.1161/CIRCRESAHA.123.323895

Developmental Cell. 2024 59:1824-1841.e10. doi: 10.1016/j.devcel.2024.04.012

Disease Models and Mechanisms. 2024 17:dmm050934. doi: 10.1242/dmm.050934

Nature Communications. 15:3931. doi: 10.1038/s41467-024-48258-5

Nature Cardiovascular Research. 2024a 3:372-388.doi: 10.1038/s44161-024-00450-y

Nature Cardiovascular Research. 2024b 3:515-524. doi: 10.1038/s44161-024-00472-6

Nature Methods. 2024. doi:10.1038/s41592-024-02534-w

Nucleic Acids Research. 2024. doi:10.1093/nar/gkae472

Stem Cell Reports. 2024 19:1053-1060. doi: 10.1016/j.stemcr.2024.06.012

2.1.4 NOVEL ARRHYTHMOGENIC MECHANISMS

Coordinator: **Silvia Priori**

Clinical leader: **David Filgueiras**

The **Novel Arrhythmogenic Mechanisms Program** aims to understand the relationship between non-arrhythmogenic phenotypes and cardiac arrhythmias in inherited animal models of cardiac disease. The program focuses on three key areas.

PHENOTYPES ELICITED BY DISRUPTION OF INTRACELLULAR CALCIUM REGULATION

Program scientists are leveraging a mouse model of Triadin-knockout syndrome, a recessive inherited disorder characterized by life-threatening diastolic arrhythmias due to the absence of triadin, a protein essential for heartbeat regulation that resides in the Ca2+ release complexes of cardiomyocytes.

Key findings in this area include:

- Electron microscopy studies revealed that mitochondria in Triadin-knockout myocytes are smaller and more abundant compared with wild-type cells, suggesting increased mitochondrial fission during disease progression (Figure 1).
- Confocal microscopy confirmed that the mitochondria of Triadin-knockout cells have a heightened tendency to accumulate Ca^{2+}, supporting the hypothesis that Ca2+ overload contributes to mitochondrial fission in Triadin-knockout syndrome.

Ongoing research is investigating the molecular factors driving mitochondrial Ca^{2+} overload in Triadin-knockout cells and how this mishandling contributes to diastolic arrhythmogenesis.

NEW TARGETS AND ADVANCED THERAPIES FOR INHERITED CHANNELOPATHIES

The program is dedicated to developing innovative concepts, tools, and therapies for inherited channelopathies, with a focus on Timothy Syndrome 1, a severe inherited arrhythmogenic disorder with a median life expectancy of less than 5 years in humans.

Using experimental data from Timothy Syndrome 1 knock-in swine myocytes and their wild-type littermates, we developed a mathematical model of ventricular cardiomyocyte electrophysiology and Ca^{2+} handling. This model successfully reproduced key Timothy Syndrome 1 phenotypes, including:

- Action potential elongation
- Cellular Ca^{2+} overload
- Increased sensitivity to early-after depolarizations (a trigger for life-threatening arrhythmias)
- Reduced depolarization reserve, a novel discovery contributing to conduction blocks

The model has also served as a predictive tool for evaluating the efficacy of current therapies (e.g., verapamil, mexiletine, ranolazine) and potential future strategies (e.g., gene therapy, IKr activators, repolarizing currents, CaMKII inhibition) (Scientific Reports, 2024).

FIBER DISORGANIZATION IN THE GENESIS OF COMMON ARRHYTHMIAS

The program has made significant contributions to integrating imaging into routine procedure planning for patients undergoing ventricular tachycardia (VT) ablation. A novel systematic strategy was developed and validated, based on scanning and processing multiple signal intensity cut-off ranges on 3D late-gadolinium enhancement cardiac magnetic resonance (LGE-CMR) images.

Key advantages of this approach include:

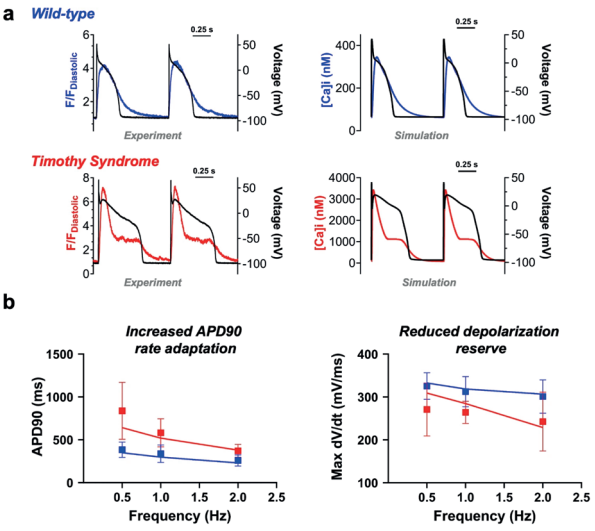
- Elimination of bias associated with manual selection of signal intensity cut-off ranges
- Simplified visualization of complex data from different myocardial layers and signal intensity cut-off ranges
- Clinically relevant assessment of infarct-related substrates and identification of myocardial regions associated with critical VT isthmus sites

This methodology is particularly valuable for planning substrate-based ablation procedures, especially in cases of unmappable VT episodes or multiple VT morphologies (Europace, 2024).

HIGHLIGHTED PUBLICATIONS

Europace. 2024 26 (10): euae244. doi: 10.1093/europace/euae244

Scientific Reports. 2024 14: 29792. doi: 10.1038/s41598-024-80726-2

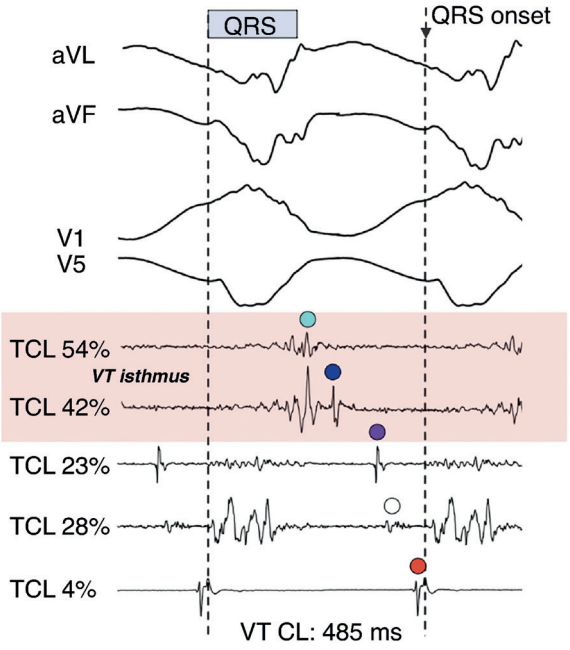


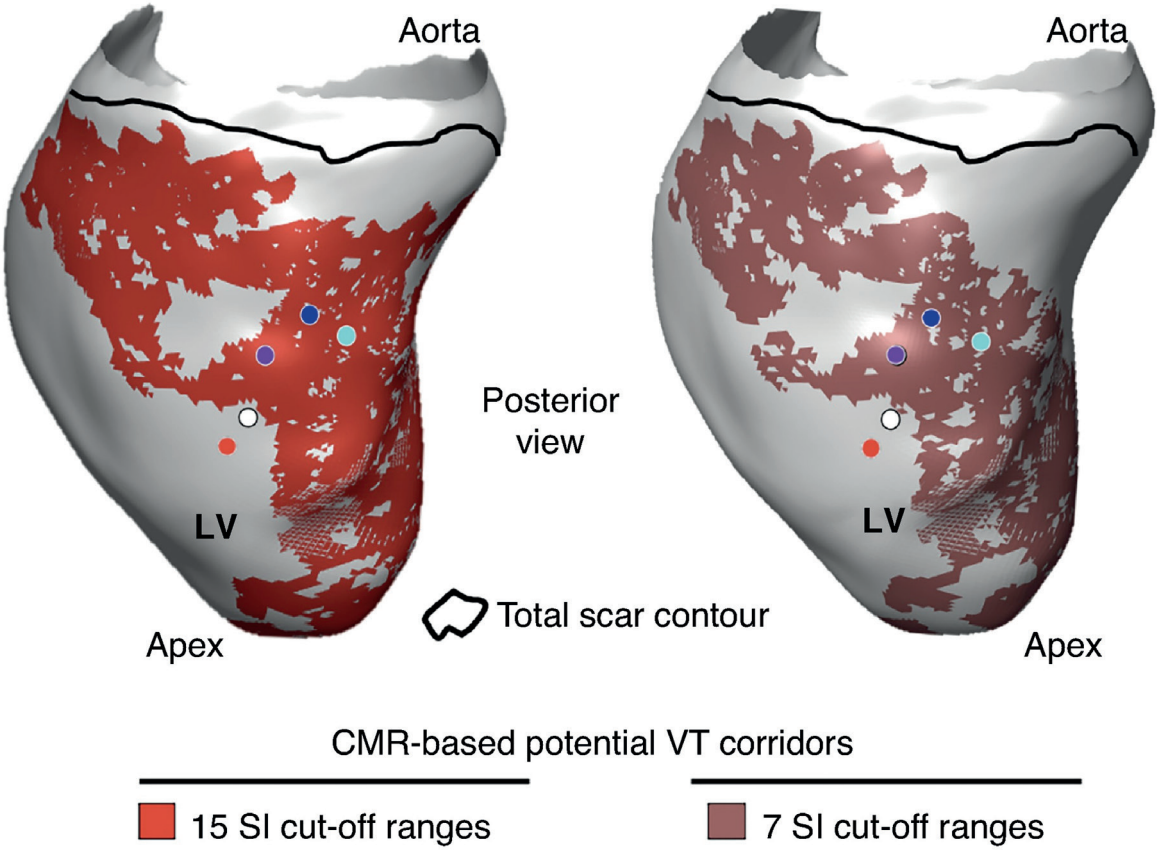
In silico modeling of the responses of ventricular myocytes from wild-type and Timothy Syndrome 1 swine. (a) Comparison between experimental (left) and simulated (right) action potentials and Ca^{2+} transients at 1 Hz pacing. Membrane voltage is plotted on the left axis, whereas cytosolic Ca^{2+} concentration (or fluorescence for experimental data) is plotted on the right axis. (b) Experimental data (squares, mean±SD) and simulated traces (lines) for action potential duration at 90% repolarization (APD90, left) and maximum upstroke velocity (Max. dV/dt), an indicator of depolarization reserve (right). Reproduced from Scientific Reports, 2024) in compliance with the terms of the article's Creative Commons Attribution 4.0 International License.

RESEARCH GROUPS

David Filgueiras
Advanced Development in Arrhythmia Mechanisms and Therapy

Silvia Priori
Molecular Cardiology





The left panels shows sample tracings during ventricular tachycardia (VT) with color-coded dots that indicate intracardiac electrograms (EGMs) at different activation times relative (%) to the tachycardia cycle length (TCL). QRS onset was used as the reference point for assigning activation times. Color-coded dots indicate different EGM–QRS times and their relative (%) activation time with respect to the TCL. The center and right panels show spatial positioning of the color-coded electrograms on the endocardial surface of the left ventricle (LV) together with corresponding imaging-derived potential VT corridors obtained at 15 (middle) and 7 (right) signal intensity (SI) cut-off ranges. Reproduced from Ramos-Prada et al. (2024), EP Europace, https://doi.org/10.1093/europace/euae244, in compliance with the terms of the article's Creative Commons Attribution 4.0 International License.

2.1.5 CARDIOVASCULAR RISK FACTORS AND BRAIN HEALTH

Coordinator: **María Ángeles Moro**
Clinical Leader: **Valentín Fuster**

The **Cardiovascular Risk Factors and Brain Health Program** investigates how cardiovascular disease and its risk factors—such as hypertension, high cholesterol, obesity, and metabolic syndrome—affect brain function. Our aim is to use this knowledge to develop strategies for preventing cerebrovascular disease and cognitive impairment with age.

KEY ACHIEVEMENTS IN 2024

PESA-Brain Study

Program members Valentín Fuster and Marta Cortes-Canteli published the rationale and design of the PESA-Brain study, which targets 1,000 participants at the 10-year follow-up PESA visit. The study includes comprehensive neuropsychological testing, advanced multimodal neuroimaging, and analysis of blood-based biomarkers of neuropathology, including Alzheimer´s disease (AD). This research is uncovering novel relationships between cardiovascular and brain alterations during the health-to-disease transition, with important implications for interventional and therapeutic approaches (American Heart Journal, 2024).

In a related, these groups found that apolipoprotein E4 (APOE4), a major genetic risk factor for AD, is also associated with an increased risk of subclinical atherosclerosis in middle age. Conversely, the APOE2 variant, which protects against AD, was shown to reduce the risk of subclinical atherosclerosis (Circulation Research, 2024a).

Brain–Body Interactions

Several groups in the Program explore brain-body interactions in health and disease. The teams led by Guadalupe Sabio (now at the CNIO) and María Ángeles Moro described how exercise activates muscle p38γ, increasing locomotor activity through the secretion of interleukin-15, which acts on the motor cortex. This mechanism plays a crucial role in reducing the risk of diabetes and liver steatosis, revealing a vital muscle–brain communication pathway with significant clinical implications for obesity and metabolic diseases (Science Advances, 2024).

Themed Issue of The British Journal of Pharmacology

Drs. Moro and Cortes-Canteli edited a themed issue of the British Journal of Pharmacology entitled ***From Alzheimer's Disease to Vascular Dementia: Different Roads Leading to Cognitive Decline*** (British Journal of Pharmacology, 2024a). This special issue reviewed several topics of core interest to Program researchers:

- The clinical evidence on the effect of anticoagulants on the development of AD and other dementias (British Journal of Pharmacology, 2024b).
- The complex interplay between microbiota and brain health, including the role of gut dysbiosis in cerebrovascular disease and its possible implications for post-stroke cognitive impairment and dementia (British Journal of Pharmacology, 2024c).
- The contribution of the peripheral myeloid lineage to AD and vascular dementia, with a special focus on post-stroke cognitive impairment (British Journal of Pharmacology, 2024d).

Additionally, María Ángeles Moro's team provided an overview of the circadian control of immune–vascular interactions both in steady-state and in pathological cardiovascular conditions, such as atherosclerosis and infarction (Circulation Research 2024b).

INTERNATIONAL ACTIONS AND RECOGNITION

During 2024, Program members participated in several international actions, including:

- **MSCA-COFUND CURE HEARTandBRAIN** (Grant Agreement 101126521; María Ángeles Moro)
- The **Leducq-funded Stroke-Impact consortium** (TNE19-CVD01) and the **Leducq Circadian Network** (TNE21-CVD04) (María Ángeles Moro)
- The **EU Joint Action on Cardiovascular Diseases and Diabetes** (JACARDI, EU4H-2022-JA-03) (Hector Bueno).

Program members also received prestigious awards, including:

- The **2024 ESC President's Award** to Hector Bueno
- The nomination of María Ángeles Moro as a **Numerary Member of the Spanish National Royal Academy of Pharmacy**.
- Ignacio Ruiz-Fernandez, from Pilar Martín's group, received the **Best Poster Presentation Award** at the 2024 CNIC Cardioimmunology meeting and the Young Investigator Award at the Heart Failure Association (ESC) Winter Meeting in Nice (April 2024).

HIGHLIGHTED PUBLICATIONS

American Heart Journal. 2024 278:195-207. doi: 10.1016/j.ahj.2024.09.028

British Journal of Pharmacology, 2024a. 181:755–759. doi: 10.1111/bph.16292

British Journal of Pharmacology, 2024b 181:760–776. doi: 10.1111/bph.16032

British Journal of Pharmacology, 2024c 181:816–839. doi: 10.1111/bph.16167

British Journal of Pharmacology, 2024d 181:777-798. doi: 10.1111/bph.16159

Circulation Research. 2024a 134(4):411-424. doi: 10.1161/CIRCRESAHA.123.323921

Circulation Research 2024b 134(6):791-809. doi: 10.1161/CIRCRESAHA.123.323619

Science Advances, 2024 10(33) eadn5993. doi: 10.1126/sciadv.adn5993

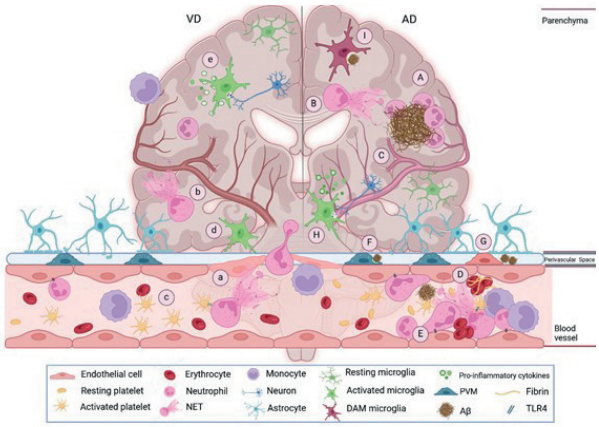
RESEARCH GROUPS

Héctor Bueno
Multidisciplinary Translational Cardiovascular Research (MTCR)

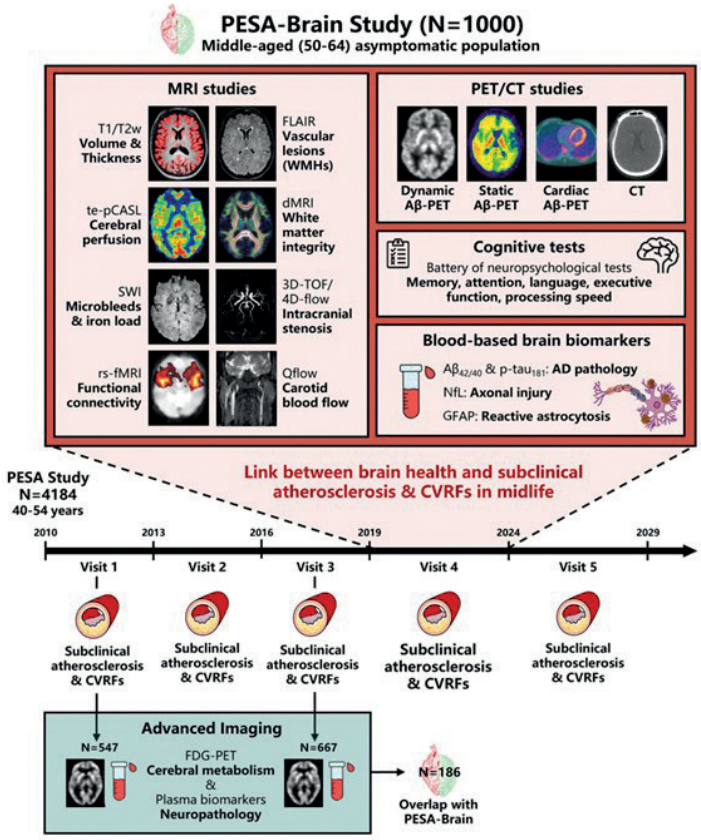
Valentín Fuster
Cardiovascular Imaging and Population Studies

Pilar Martín
Regulatory Molecules of Inflammatory Processes

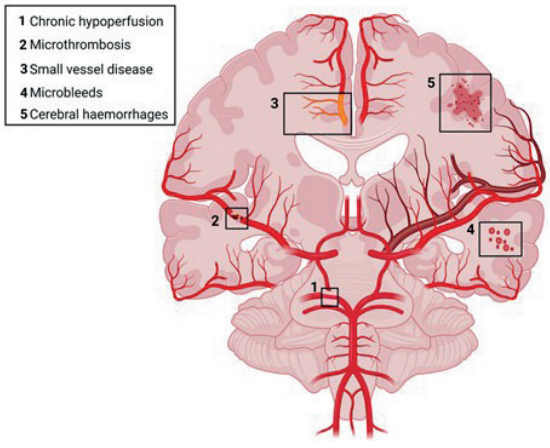
María Ángeles Moro
Neurovascular Pathophysiology



Effects of myeloid cells in Alzheimer's disease (AD) and vascular dementia (VD).
AD: (A) Neutrophils infiltrate the brain parenchyma located close to amyloid-β (Aβ) plaques. (B) These infiltrating neutrophils are activated by inflammatory mediators (possibly released by microglia) and can produce neutrophil extracellular traps (NETs). (C) Monocytes may participate directly in the removal of Aß-plaques. (D) NETs are also produced by neutrophils adhered to the vessel wall; production of these intravascular NETs may involve a contribution from activated platelets via TLR4. E) Platelets may also be responsible for the accumulation of Aβ in blood clots inside and around cerebral blood vessels. (F) Aβ phagocytosis in the perivascular space by perivascular macrophages (PVMs). (G) Intravascular Aβ crosses the vessel wall, enters the perivascular space, reaches PVMs, induces ROS production, and alters neurovascular function. (H) Excessive microglia activation causes neurotoxicity and synaptic loss. (I) Disease-associated microglia (DAM) involved in Aβ clearing.
VD: (a) Parenchymal and (b) intravascular NETs impair vascular remodeling during stroke recovery. (c) Platelet activation is still present in the chronic phase of ischemic stroke. (d) Vessel-attached microglia play a beneficial role in maintaining blood–brain barrier (BBB) integrity. (e) Activation of harmful microglia leads to pro-inflammatory cytokine release and the phagocytosis of astrocyte endfeet and axons, aggravating BBB damage.
(Figure modified from British Journal of Pharmacology, 2024d)



PESA-Brain Study Design.
Imaging Techniques: FLAIR, fluid-attenuated inversion recovery; MRI, magnetic resonance imaging; mS-DTI, multishell diffusion tensor imaging; PET, positron emission tomography; rs-fMRI, resting-state functional MRI; SWI, susceptibility-weighted MRI; te-pCASL, time-encoded pseudo-continuous arterial spin labeling; TOF, time-of-flight.
Biomarkers: Aβ42/40, amyloid-β ratio 42/40; FDG, [18F] fluorodeoxyglucose; GFAP, glial fibrillary acidic protein; NfL, neurofilament light chain; p-tau181, phosphorylated tau 181.
Conditions: AD, Alzheimer's disease; CVRF, cardiovascular risk factor.



Pathophysiological processes of vascular origin in vascular cognitive impairment.
1. Chronic hypoperfusion: Reduced blood flow and oxygen supply due to conditions like chronic hypertension or atherosclerosis.
2. Microthrombosis: Formation of small blood clots in brain vessels.
3. Small vessel disease: Characterized by damage to small blood vessels, reducing blood flow.
4. Microbleeds: Rupture of small brain vessels due to hypertension or cerebral amyloid angiopathy.
5. Cerebral hemorrhages: Bleeding in the brain from ruptured blood vessels.
(Figure modified from British Journal of Pharmacology, 2024d)

2.1.6 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 diets, and physical inactivity. Alarmingly, the problem is expected to worsen 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, aiming to implement early prevention strategies and develop noninvasive technologies to support translational research and population studies on preclinical atherosclerosis.

The ultimate goal of the CHPP is to reduce the personal and societal burden of CVD through health promotion and prevention strategies, potentially increasing life expectancy and reducing the risk of other diseases, such as dementia and cancer. The program focuses on three key objectives:

Refining primordial prevention strategies in children and adolescents.

Improving global primary prevention by addressing the subclinical development and progression of atherosclerosis in young adults.

Translating health promotion initiatives to the general population.

The CHPP comprises 2 research groups: Cardiovascular Imaging and Population Studies (PI, Valentin Fuster) and Cardiovascular Health and Imaging (PI, Rodrigo Fernández-Jiménez). In 2024, the program achieved significant scientific advances, highlighted below.

KEY ACHIEVEMENTS IN 2024

SI! Program for Elementary Schools Trial Results

CHPP scientists reported the primary results of the SI! Program for Elementary Schools trial, a 6-year cluster randomized intervention in 48 state-funded elementary schools in the Madrid region. The trial evaluated the impact of time-varying exposures to a multicomponent school-based health promotion program. Children exposed to the SI! Program throughout all 6 elementary school years or during the first 3 elementary school years showed significant improvements in abdominal adiposity markers (Figure 1) (Journal of the American College of Cardiology, 2024a).

Addressing Health Disparities in Adolescents

Analysis of data from the SI! Program for Secondary Schools trial revealed that adolescents from low socioeconomic backgrounds and migrant families were more likely to belong to groups with poorer cardiovascular health trajectories. These groups also had the highest prevalence of overweight/obesity and metabolic syndrome, underscoring the need for primordial prevention interventions targeting vulnerable populations (Figure 2) (Journal of Adolescent Health, 2024).

Sex-Specific Reference Values for Cardiac Strain in Adolescents

CHPP researchers established sex-specific reference values for biventricular strain using magnetic resonance imaging in adolescents aged 15 to 18 years. These values provide a valuable tool for detecting subtle changes at subclinical disease stages in pediatric populations (Journal of Magnetic Resonance Imaging, 2024).

Collaborative Program Highlights

Subclinical Atherosclerosis and Mortality

In collaboration with other CNIC research programs, CHPP researchers analyzed data from the BioImage study, demonstrating that subclinical atherosclerosis burden and progression in asymptomatic individuals were independently associated with all-cause mortality (Figure 3) (Journal of the American College of Cardiology, 2024b).

Apolipoprotein E and Cardiovascular Disease

Through analysis of data from the PESA study, CHPP researchers uncovered the role of apolipoprotein E in cardiovascular disease development, offering important insights for therapeutic and prevention strategies, particularly in early midlife (Circulation Research, 2024).

Outreach and Recognition

The CHPP recognizes the importance of effective communication to raise public awareness of cardiovascular health and healthy lifestyles. In 2024, program scientists participated in outreach activities, including the XXIV Science and Innovation Week in Madrid.

Additionally, CHPP researchers received prestigious awards, including:

The Gabriella Morreale National Youth Research Award in Medicine and Health Sciences, awarded to Dr. Rodrigo Fernandez-Jimenez by the Ministry of Science, Innovation, and Universities.

The Lifetime Achievement Award by the World Heart Federation, the AstraZeneca Foundation Honorific Award for Excellence in Scientific Research, and the Antonio M. Gotto Jr. Prize in Atherosclerosis Research by the International Atherosclerosis Society, all awarded to Dr. Valentin Fuster.

HIGHLIGHTED PUBLICATIONS

Circulation Research. 2024 134(4):411-424. doi: 10.1161/CIRCRESAHA.123.323921

Journal of Adolescent Health. 2024;74(5):1039-1048. doi: 10.1016/j.jadohealth.2023.12.016

Journal of Magnetic Resonance Imaging. 2024 60(6):2409-2420. doi: 10.1002/jmri.29334

Journal of the American College of Cardiology. 2024a 84(6):499-508. doi: 10.1016/j.jacc.2024.04.065

Journal of the American College of Cardiology. 2024b 84(15):1391-1403. doi: 10.1016/j.jacc.2024.06.045

RESEARCH GROUPS

Rodrigo Fernández-Jiménez
Cardiovascular Health and Imaging

Valentín Fuster
Cardiovascular Imaging and Population Studies

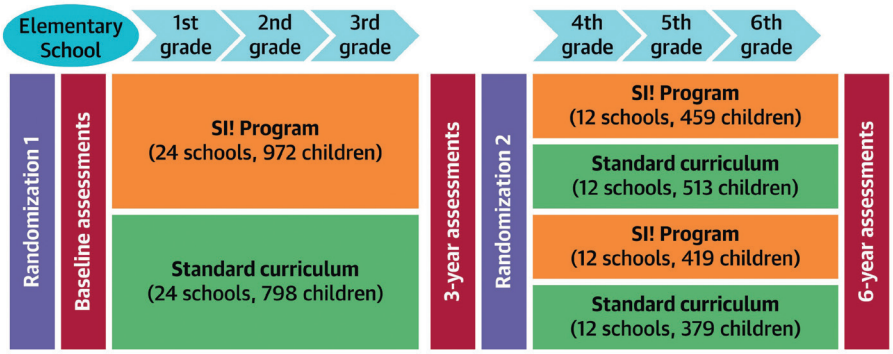


Figure 1. Study design of the SI! Program for Elementary Schools trial. The SI! Program curriculum covers diet, physical activity, body and heart health, and emotional management. The curriculum was implemented for the first 3 years (grades 1-3), the final 3 years (grades 4-6), or throughout all 6 years of elementary school. Control schools followed the standard curriculum. Primary outcomes included changes in adiposity markers. Reproduced from J Am Coll Cardiol, 2024a.

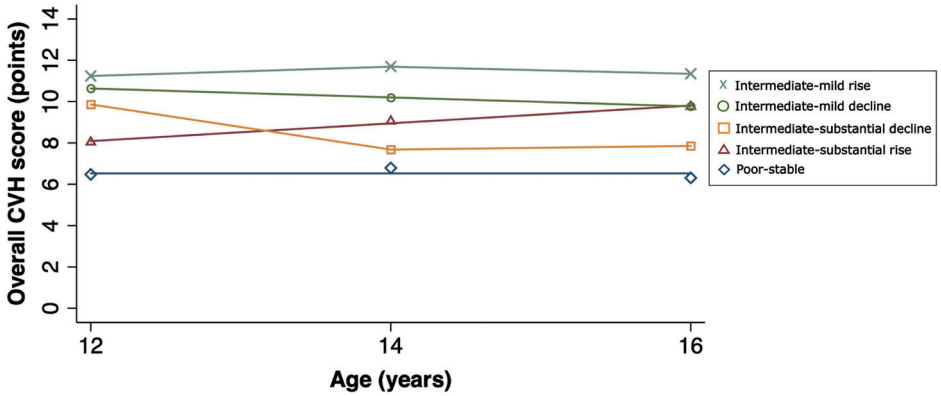


Figure 2. Cardiovascular health trajectories in adolescence. Based on American Heart Association thresholds, cardiovascular health (CVH) metrics (smoking, BMI, physical activity, diet, blood pressure, cholesterol, and blood glucose) were scored as 0 (poor), 1 (intermediate), or 2 (ideal). The overall CVH score thus ranged from 0 to 14 points, with higher scores indicating better CVH. Trajectories are ordered by baseline CVH scores. Reproduced from J Adolesc Health, 2024.

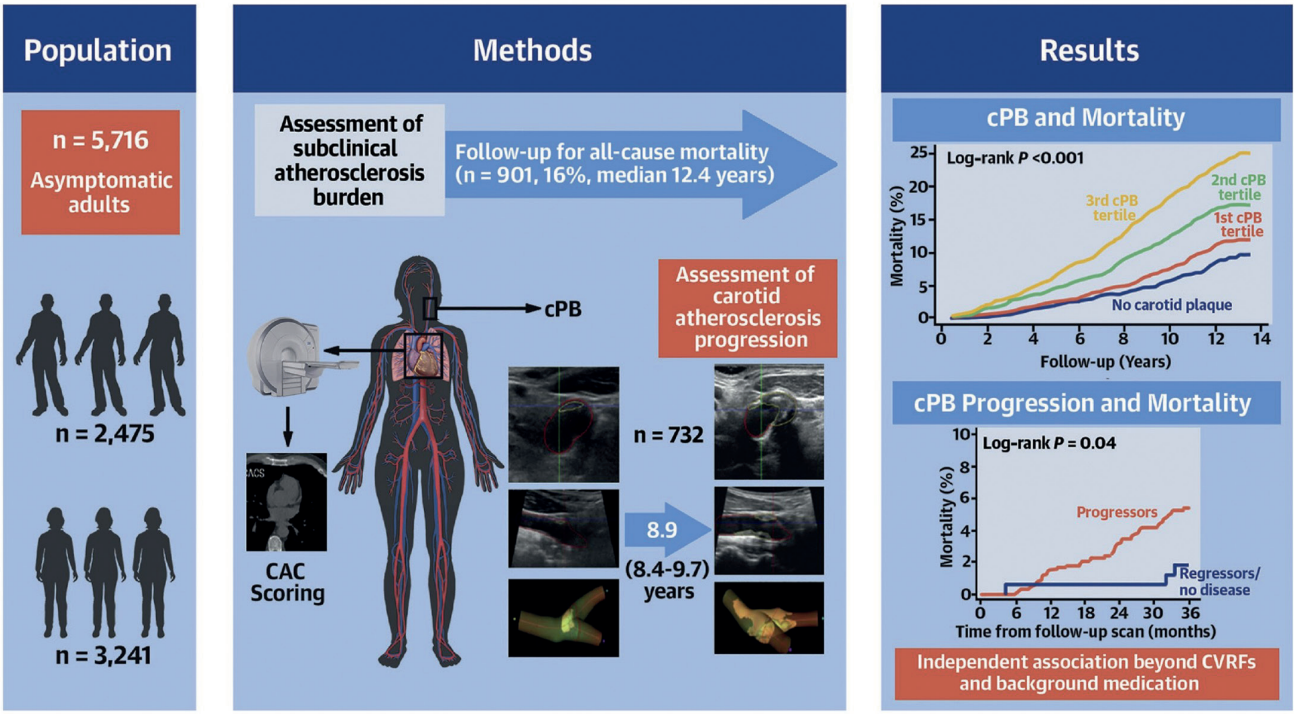


Figure 3. Study design and main results of the BioImage study. The study enrolled 5,716 asymptomatic individuals assessed for subclinical atherosclerosis (coronary artery calcium [CAC] score and carotid plaque burden [cPB]) and cardiovascular risk factors (CVRFs). A subset of 732 participants were reassessed after 8.9 years. Atherosclerosis burden and the progression of carotid atherosclerosis were independently associated with all-cause mortality. Reproduced from J Am Coll Cardiol, 2024b.

2.1.7 TECHNOLOGY DEVELOPMENT

Coordinator: **Beatriz Álvarez**

The **Technology Development Program** (TDP) comprises 11 Technical Units (TUs) that keep the center at the forefront of cardiovascular research by developing and implementing cutting-edge biomedical technologies. The TUs provide internal and external services, engage in training, and participate in scientific collaborations through funded projects. More information about the TUs can be found at https://www.cnic.es/en/investigacion/unidades-tecnicas.

Advanced imaging capabilities support detailed molecular and anatomical visualization, enabling comprehensive studies from whole-organ to cellular resolution. These efforts are complemented by units focused on cellular engineering and gene editing, which develop innovative genetically modified models—including large animal systems—to unravel disease mechanisms with high precision. Omics platforms, including cytometry, proteomics, and genomics, offer in-depth cellular and molecular characterization, while the bioinformatics infrastructure enables integration and analysis of complex datasets, driving data-driven discoveries. Collaborative developments in gene therapy vectors exemplify the translational potential emerging from this research framework. Together, these interconnected units form a dynamic and innovative environment that accelerates the transition from basic research to clinical applications, reinforcing the CNIC's leadership in cardiovascular science.

KEY ACHIEVEMENTS IN 2024

ISO Certification: All TUs obtained UNE-EN-ISO 9001:2015 certification, guaranteeing the quality of services and continuous process improvement.

High-Tech Equipment Acquisition: The TDP successfully acquired all five items requested in the competitive EQC2024 call, resulting in a total economic saving of €2.7 million for the center. The new equipment includes:

A high-tech axial computerized tomography system with a spectral detector.

A high-sensitivity mass spectrometer coupled to ultra-high-pressure liquid chromatography for metabolomics and targeted lipidomics.

A 3-4D multimodal-adaptive fluorescence microscope.

An expansion of the center's computing capacity with a new platform for the storage and analysis of biomedical images using artificial intelligence (AI).

Two newly acquired cutting-edge ultrasound imaging systems

TRAINING AND KNOWLEDGE DISSEMINATION

Training is a core activity at the CNIC, and the TDP is committed to supporting it through several actions:

Participation of the the TUs in the UAM Master's in Molecular Biomedicine (BMM7).

Involvement in scientific training and communication programs, such as Acércate and Res@cnic, as well as the seminar program.

Organization of Technodays, a 3-day event for sharing scientific and technical expertise. The 2024 edition focused on three key areas:

1. In Vivo and In Vitro Models
2. Omics
3. Cardiac and Brain Imaging

Coordination (by the Microscopy Unit) of the scientific committee of the SPAOM2024 congress (Spanish & Portuguese Advanced Optical Microscopy Meeting, Toledo, Nov 2024).

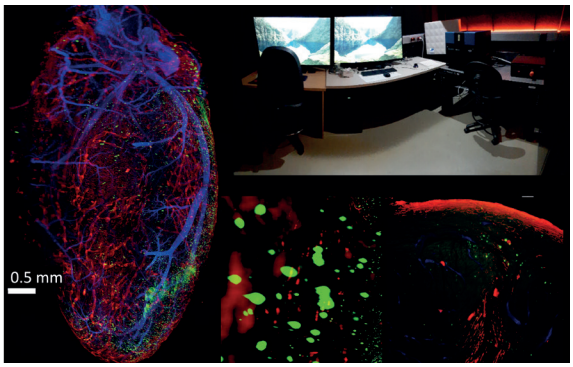
SCIENTIFIC OUTPUT IN 2024

The CNIC TUs contributed to the center's scientific production, with 102 articles published—accounting for 26% of the center's total output.

82% of publications appeared in first-quartile journals

42% were featured in first-decile journals.

47% were the result of international collaborations.



Microscopy analysis suite and images of a mouse heart labeled for endothelial cell nuclei (green), microvasculature (red), and arteries (blue). The heart images were generated in collaboration with Luis Diago and Rui Benedito of the Molecular Genetics of Angiogenesis Laboratory.

TECHNICAL UNITS

Fátima Sánchez Cabo
Bioinformatics

Antonio J. Quesada
Clinical Trial Coordination

Comparative Medicine

Beatriz Álvarez
Flow Citometry

Ana Dopazo
Genomics

Manuel Desco
Imaging

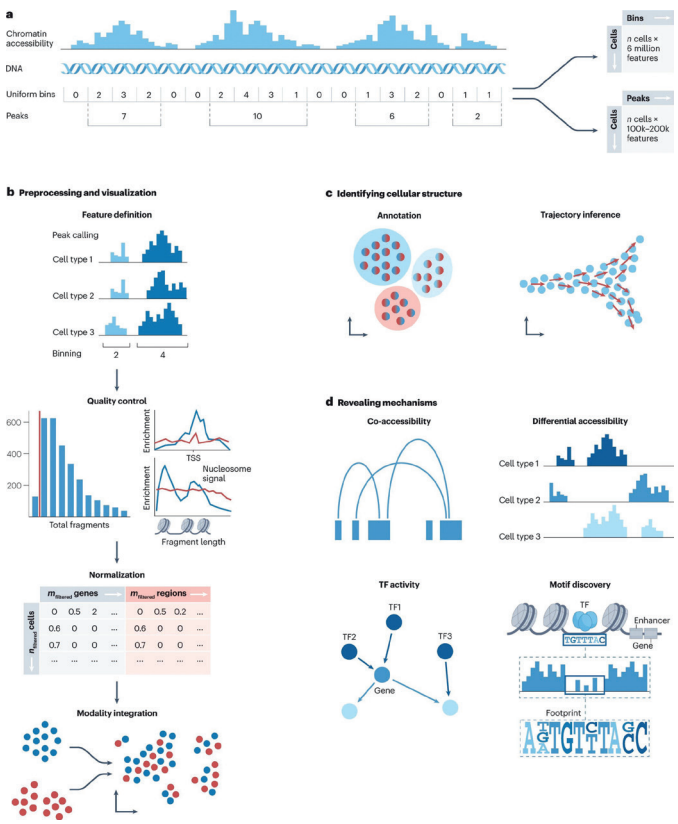
Valeria Caiolfa
Microscopy

Giovanna Giovinazzo
Pluripotent Cell Technology

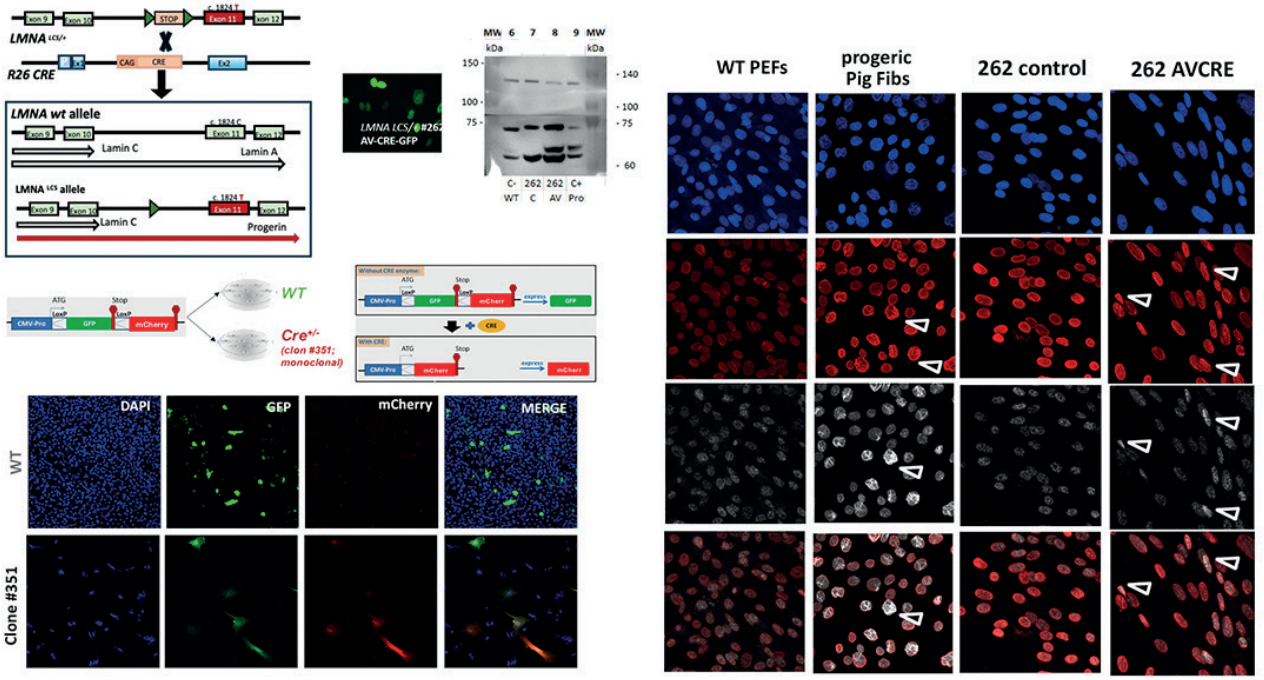
Juan Antonio López
Proteomics

Juan De Dios Hourcade
Transgenesis

Juan A. Bernal
Viral Vectors



Single-cell assay for transposase-accessible chromatin using sequencing (scATAC-seq) is a method for measuring chromatin accessibility in individual cells.



Design of gene editing strategies based on the CRISPR/Cas9 system and critical experiments for generating models of cardiovascular disease, in vivo models and in vitro models in hiPSCs.

2.2 CLINICAL STUDIES AT THE CNIC

Clinical-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.

Clinical-translational research is a cornerstone of our work at the CNIC. We are committed to advancing these studies and ensuring their impact on patient care. Below, we highlight some of the clinical projects that were active in 2024.

PESA-HEALTH-CNIC-SANTANDER: EARLY DETECTION OF SUBCLINICAL ATHEROSCLEROSIS, DISEASE PROGRESSION, AND CARDIOVASCULAR HEALTH

Principal Investigator: *Valentín Fuster*

PESA Health Initiative

cnic Santander

The PESA-Health-CNIC-Santander study builds on the foundation laid by its predecessor, the PESA Study, which began in 2010 under the direction of the CNIC in collaboration with Santander Bank. The original study enrolled 4,184 asymptomatic individuals aged 40 to 55 and aimed to detect subclinical atherosclerosis (SA) long before symptoms appear, while also exploring the factors driving its development and progression.

The continuation of the PESA study, PESA-Health, extends this work by tracking the same participants over an additional 10 years. The new study broadens the scope to include new research areas, such as the links between SA and Alzheimer's disease or cognitive decline, the role of somatic mutations in aging, and how these mutations may influence cardiovascular events and SA progression.

As in the original PESA study, PESA-Health leverages advanced imaging technologies, including 3D vascular ultrasound of the carotid arteries and aorta, coronary artery calcium quantification via computed tomography, cardiac magnetic resonance, AngioTC, PET, and PET-amyloid analysis. In addition, biosampling is used for for extensive omics analysis, and new substudies are exploring the connection between SA and sleep apnea.

As the CNIC's flagship study, PESA-Health involves many of the center's clinical and basic research groups. Findings from the PESA study have already made significant contributions to understanding the origins and progression of atherosclerosis.

PESA-Health launched in February 2020, with 3,496 PESA participants continuing their involvement. By the end of 2024, the first round of visits was completed for 3,300 individuals, and the second round of visits had begun.

RESILIENCE: REMOTE ISCHEMIC CONDITIONING IN LYMPHOMA PATIENTS RECEIVING ANTHRACYCLINES

Principal Investigator: *Borja Ibáñez*
H2020 Grant# 945118

RESILIENCE

Anthracyclines are a widely used class of anticancer drugs, administered to over 3 million of the 4 million new cancer patients diagnosed annually in Europe. While effective, these drugs carry a significant risk: recent data show that >35% of patients treated with anthracyclines develop some form of cardiomyopathy. This trade-off between cancer treatment and chronic heart failure (HF) not only places a heavy psychological burden on cancer survivors but also poses a growing challenge for healthcare systems.

Remote ischemic pre-conditioning (RIPC) offers a potential solution. RIPC is a noninvasive, safe, and cost-effective technique that involves brief, reversible episodes of ischemia (e.g., in an arm) followed by reperfusion. This process can protect remote tissues and organs against injury in future ischemic events. Experimental studies in large animals have shown that 3 to 5 cycles of 5-minute limb ischemia followed by 5-minute reperfusion reduce the size of induced myocardial infarctions. Recent evidence suggests that, to be effective, RIPC must be initiated before the damaging event. Since chemotherapy is a planned procedure, anthracycline-induced cardiomyopathy provides an ideal setting to test this approach.

RESILIENCE is a multinational, phase II, double-blind, sham-controlled, randomized controlled trial evaluating the efficacy and safety of RIPC in patients with lymphoma or breast cancer and who are receiving anthracyclines. Eligible patients scheduled to receive ≥240 mg/m² of anthracyclines undergo baseline cardiac magnetic resonance (CMR) imaging and blood tests for high-sensitivity troponin (hsTn) and NT-proBNP. Patients with a left ventricular ejection fraction >40% confirmed by CMR are randomized 1:1 to receive either RIPC or a sham procedure.

Nine weeks after completing chemotherapy, patients undergo a final CMR and hsTn/NT-proBNP test. Clinical follow-ups are scheduled for 12, 18, 30, and 42 months until the last patient completes the final CMR.

The RESILIENCE 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-945118-RESILIENCE), the trial began its grant period in June 2021, with patient recruitment starting in 2022. By the end of 2024, three additional

hospitals were added, all 22 sites were operational, and 284 participants had been enrolled.

REBOOT: TREATMENT WITH BETA-BLOCKERS AFTER MYOCARDIAL INFARCTION WITHOUT REDUCED EJECTION FRACTION

Principal Investigator: *Borja Ibáñez*

The use of beta-blockers for patients after a myocardial infarction (MI) is largely based on evidence from trials conducted before the reperfusion era. While these drugs have proven benefits for post-MI patients with reduced ejection fraction, their effectiveness for patients with preserved ejection fraction remains unclear. Despite this lack of evidence, over 80% of post-MI patients in this category are prescribed beta-blockers for life.

The REBOOT trial addresses this gap by evaluating the need for beta-blocker therapy in post-MI patients with a left ventricular ejection fraction greater than 40%. This multinational study has enrolled 8,506 patients, who have been randomized to either receive beta-blockers (with the type and dose determined by their physician) or no beta-blocker treatment. The primary endpoint is a composite of all-cause death, reinfarction, or heart failure admission over a 3-year follow-up period.

Coordinated by the CNIC Clinical Trials Coordination Unit and conducted in collaboration with the Mario Negri Institute of Pharmacological Research in Milan, the trial involves 77 hospitals in Spain and 29 in Italy. This large-scale project has the potential to significantly influence clinical practice.

Patient enrollment began in October 2018 and has now been completed. The trial is currently in the event-adjudication process.

MRVALVE: MULTIMODALITY MYOCARDIAL TISSUE CHARACTERIZATION IN PATIENTS WITH SIGNIFICANT VALVULAR DISEASE

Principal Investigator: *Borja Ibáñez*

The MRVALVE study uses a multimodality imaging approach (cardiac magnetic resonance [CMR] and strain echocardiography) to better characterize left ventricular (LV) status in patients with significant valvular heart disease (VHD), focusing on aortic valve stenosis (AS) as a model of LV pressure overload and mitral regurgitation (MR) as a model of LV volume overload.

VHD significantly impacts LV dimensions, function, and tissue composition, all of which play a critical role in clinical decision-making. Current guidelines recommend surgical treatment for patients with significant VHD when symptoms develop or when there is evidence of LV remodeling or dysfunction. The most common forms of VHD are AS and MR. The progression from asymptomatic to symptomatic disease, or from normal LV function to LV dilatation, hypertrophy, and dysfunction, is driven by changes in tissue composition—primarily cardiomyocyte death, extracellular volume expansion, and fibrosis.

While surgery or percutaneous valve repair or replacement are effective treatments for severe VHD, interventions are typically based on the presence of symptoms or significant LV dysfunction. By the time these features appear, it is often too late to fully restore heart function. This highlights the need for tools for the early detection of myocardial involvement in asymptomatic VHD patients, allowing timely intervention before irreversible damage occurs.

CMR is the gold standard for anatomical and functional cardiac assessment. This methodology can detect focal fibrosis through late gadolinium enhancement and offers advanced tissue characterization using techniques like parametric T1/T2 mapping, absolute myocardial perfusion quantification, and extracellular volume calculation (a marker of diffuse fibrosis). These assessments require the use gadolinium-based contrast agents, which have a strong safety profile and are widely used in clinical practice. A blood sample is also needed to determine hematocrit for assessing diffuse fibrosis.

Strain echocardiography, the best imaging modality for evaluating active LV myocardial deformation, can detect impaired multidirectional strain even when overall LV function appears normal. In the MRVALVE study, we correlate imaging data with functional assessments from the 6-minute walking test, which provides an objective measure of exercise capacity. Additionally, cardiac computed tomography is used to assess calcium deposition in the coronary arteries and heart valves, providing a calcium score that serves as both a diagnostic and prognostic tool in AS patients.

To date, 71 patients have been recruited, 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#819775

The MATRIX Project aims to develop innovative treatments for cardiotoxicity caused by certain cancer therapies. This initiative is a joint effort between the CNIC and ***Fundación Jiménez Díaz*** University Hospital, building on a collaborative framework established in 2015 to study myocardial diseases.

While significant advances in cancer treatment have improved outcomes for the 4 million new cancer patients diagnosed annually in Europe, these therapies often come with serious side effects. One of the most common is cancer treatment–induced cardiotoxicity (CTiCT), which affects up to 25% of patients treated with anthracyclines or trastuzumab. CTiCT can lead to severe complications, including chronic heart failure or even death, creating a devastating trade-off for cancer survivors.

CTiCT poses a significant challenge, as current therapies are suboptimal. Early detection methods are inadequate, and heart failure treatments are nonspecific. Recent findings from our group suggest that CTiCT is linked to altered mitochondrial dynamics, which triggers metabolic reprogramming in cardiomyocytes.

The MATRIX Project takes a holistic approach to addressing mitochondrial dysfunction in CTiCT. We propose that early-stage CTiCT could be reversed by metabolic reprogramming to alter mitochondrial substrate utilization. Using a novel imaging-based algorithm developed by our team, we aim to detect myocardial damage in patients receiving common anticancer drugs long before traditional clinical parameters show abnormalities. This early detection, currently unavailable, is critical for timely intervention.

For end-stage CTiCT, where mitochondrial dysfunction may be irreversible, we propose that replenishing the myocardium with healthy mitochondria through in-vivo mitochondrial transplantation could offer a radical new therapeutic option.

The MATRIX Project has broad translational potential, including the development of new therapeutic approaches, early diagnostic technologies, and insights into the basic mechanisms of CTiCT.

Patient recruitment began in 2020, and as of February 2025, 56 participants have been enrolled.

MYOCARDITIS-CNIC: PROSPECTIVE REGISTRY TO VALIDATE A NEW DIAGNOSTIC MARKER IN PATIENTS WITH CLINICAL SUSPECT OF MYOCARDITIS

Principal Investigator: *Pilar Martín Fernández*
Co-Principal Investigator: *Domingo Pascual Figar*

Acute myocarditis is challenging to diagnose due to its varied clinical presentation and the lack of rapid, accessible, and accurate diagnostic tools. Symptoms can range from atypical chest pain (resembling pericarditis or angina) to dyspnea, fatigue, palpitations, syncope, and, in severe cases, sudden death or shock. Early diagnosis is further complicated by the nonspecific results obtained with standard tests, such as ECG, echocardiography, and laboratory tests.

Currently, diagnosing acute myocarditis typically requires invasive procedures like endomyocardial biopsy or advanced imaging techniques like cardiovascular magnetic resonance, which are not universally available. This highlights the urgent need for new, noninvasive diagnostic approaches.

Dr. Martín Fernández's research group has made significant progress in this area by identifying a novel microRNA in mice and humans with myocarditis. Their work, published in the New England Journal of Medicine (2021: 27;384(21):2014-2027), demonstrates that the human homolog (hsa-miR-Chr8:96) can effectively distinguish myocarditis patients from those with myocardial infarction.

The MYOCARDITIS-CNIC Registry, a collaborative initiative between the CNIC and ***Hospital Virgen de la Arrixaca***, aims to build on these findings. Several Spanish hospitals, including ***Hospital de la Princesa*** and ***Clínica Universitaria de Navarra***, are participating in the registry by collecting clinical data and biological samples from patients presenting to emergency departments with signs of myocarditis. This registry will provide critical insights into the early stages of myocarditis and help validate potential clinical biomarkers for early diagnosis.

To date, 75 participants have been enrolled in the registry.

PRECOGNITIVE: EFFECT OF REMOTE ISCHEMIC PRECONDITIONING ON COGNITIVE FUNCTION AND CEREBRAL VASCULATURE

Principal Investigator: *Gonzalo Pizarro Sánchez*

Arterial hypertension can cause damage to the cerebral vascular system, even when blood pressure effectively controlled. Current treatments for hypertension focus on managing blood pressure and preventing damage to target organs, such as the brain. Remote ischemic preconditioning (RIPC), a technique first shown to protect organs like the heart and brain in animal models 30 years ago, has since been adapted for use in human patients. RIPC involves inflating and deflating a blood pressure cuff on the arm through four cycles of 5 minutes each. The brief ischemia induced in the arm can protect distant organs, including the brain, from future ischemic damage.

Our research group has contributed significantly to this field, with recent studies demonstrating that RIPC can improve cognitive performance and cerebral vascular function in patients with vascular dementia.

The PRECOGNITIVE study is a proof-of-concept randomized trial involving 45 women with hypertension and evidence of target organ damage, such as left ventricular hypertrophy. Participants are divided into 3 groups:

1. The RIPC group undergo the RIPC procedure, with the cuff inflated to 20 mmHg above their systolic blood pressure.
2. The RIPC-Sham group follow the same procedure, but the cuff will only be inflated to 50 mmHg, insufficient to induce ischemia.
3. The control group do not receive any cuff therapy.

The study aims to determine whether RIPC has a significant protective effect on the cerebral vasculature in hypertensive patients without significant cognitive impairment. Outcomes will be assessed using comprehensive neurocognitive tests and noninvasive imaging techniques, including echocardiography, noncontrast brain magnetic resonance imaging, and transcranial Doppler ultrasound.

As of the end of 2024 15 patients have been recruited.

MACADAMIA: CHARACTERIZATION OF CARDIAC METABOLISM USING MULTIMODAL IMAGING IN IDIOPATHIC CARDIOMYOPATHY

Principal Investigator: *Borja Ibáñez*

Heart failure (HF) is one of the most significant health challenges in modern societies, placing a heavy burden on healthcare systems. To develop new therapies, it is essential to understand the mechanisms underlying the development and progression of HF.

The heart is the body's most energy-demanding organ relative to its size. Under normal conditions, it primarily relies on fatty acid beta-oxidation, which generates about 60% of the ATP needed for cardiac function. Carbohydrate metabolism via the Krebs cycle provides the second-largest energy source, while other nutrients, such as amino acids, contribute less than 1%.

In HF, however, the heart undergoes a metabolic shift, switching from fatty acids to glucose as its main energy source. This phenomenon, known as the metabolic switch, was initially thought to be a protective adaptation. However, recent evidence from animal and human studies shows that glucose metabolism produces 4-5 times less ATP than fatty acid metabolism, suggesting that this switch is harmful and contributes to the decline in cardiac contractile function.

Our group has demonstrated that the metabolic switch plays a key role in the progression of HF secondary to idiopathic dilated cardiomyopathy (IDCM). In mouse models, a diet rich in fatty acids reversed the metabolic switch and improved the IDCM phenotype. Similar results were observed in pigs, which have a metabolism comparable to humans.

Before conducting a clinical trial in patients with IDCM, it is critical to determine the prevalence of the metabolic switch in this population. This is the primary goal of the MACADAMIA study, an observational project involving a small cohort of IDCM patients. Using advanced imaging techniques—including transthoracic echocardiography with myocardial strain analysis, cardiac magnetic resonance (CMR), and positron emission tomography/computed tomography (PET/CT) with the radiotracer 18FDG—the study aims to characterize the metabolic profile of these patients without any intervention.

As of February 2025, 28 patients have been recruited. In the medium to long term, we plan to conduct a clinical trial in IDCM patients who exhibit the metabolic switch. Patients will be randomized to receive either a diet rich in fatty acids or a normal diet, and will be assessed for changes in cardiac function (by CMR) and metabolism (by PET/CT).

ATTRACKING CNIC: THE ATTRACKING REGISTRY

Principal Investigator: *Pablo García Pavía*

Tafamidis is a medication used to treat transthyretin cardiac amyloidosis (ATTR-CM), a rare and life-threatening disease caused by the buildup of of transthyretin amyloid fibrils in the heart. Clinical trials have demonstrated that Tafamidis reduces mortality and cardiovascular hospitalizations in patients with ATTR-CM, prompting its recent approval for use in Spain. However, clinical trials can have limitations, and their results may not always reflect real-world clinical outcomes.

Advances in diagnostic techniques have enabled earlier detection of ATTR-CM, resulting in a shift in patient profiles and improved prognoses compared with the population studied in the original clinical trial. This raises questions about the effectiveness and safety of Tafamidis in contemporary patients. The ATTRACKING CNIC study aims to address this uncertainty by evaluating Tafamidis in a real-world, unselected cohort of ATTR-CM patients.

Objectives

1. To characterize the real-world population of ATTR-CM patients in Spain prescribed 61mg Tafamidis.
2. To assess the safety of Tafamidis in a diverse, real-world Spanish cohort with ATTR-CM.
3. To compare the real-world clinical impact of Tafamidis therapy with the results of the ATTR-ACT clinical trial.

Study Design

ATTRACKING CNIC is a prospective, multicenter, non-randomized observational trial involving patients diagnosed with ATTR-CM who are starting daily treatment with 61 mg Tafamidis.

As of February 2025, contracts have been signed with 22 hospitals, and 195 participants have been recruited.

TAILOR-AF: PATIENT-SPECIFIC ABLATION OF PERSISTENT ATRIAL FIBRILLATION DRIVERS GUIDED BY FREQUENCY AND AMPLITUDE MODULATION CRITERIA

Principal Investigator: *David Filgueiras*
Co-Promoter: *Hospital Universitario Clínico San Carlos*

Pulmonary vein isolation (PVI) is the cornerstone of catheter-based ablation for patients with persistent atrial fibrillation (AF). However, over the past 20 years, the success rate of PVI in achieving long-term rhythm control for persistent AF has been suboptimal. Even with treatment, only about 40% of patients remain free of AF (without antiarrhythmic drugs) at 12 months post-ablation, highlighting the challenges of managing this condition.

To address this issue, our group has developed a computational tool that helps interventional electrophysiologists identify specific atrial regions, called driver regions, which are associated with the long-term persistence of AF. Using a conventional electroanatomic mapping system and multielectrode catheters, these regions can be pinpointed with novel signal processing algorithms. These algorithms, which are openly available to the scientific community (Quintanilla JG et al. Circ Res. 2019;125:609-27), analyze individual atrial signals to detect frequency and amplitude modulations (iFM and iAM) during fibrillatory activity. This allows for the precise localization of rotational activity and the identification of the leading drivers of persistent AF.

The primary goal of the TAILOR-AF study is to use iAM/iFM mapping to identify and ablate the leading drivers of AF in patients who continue to experience symptomatic recurrences of persistent AF despite undergoing 2 or more PVI procedures. Secondary objectives include analyzing blood biomarkers, atrial imaging parameters, and phenotypic features in the surface electrocardiograms associated with advanced atrial remodeling. In patients undergoing minimally invasive thoracoscopy-guided ablation of leading drivers, tissue samples from the left atrial appendage will also be collected to study the molecular mechanisms underlying AF maintenance.

As of the end of 2024, 22 patients had been enrolled in the study.

SIR-CVT: SPANISH IMMUNOTHERAPY REGISTRY – CARDIOVASCULAR TOXICITY

Co-Promoters: *Sociedad Española de Cardiología / Sociedad Española de Oncología Médica*

SIR-CVT
Spanish Immunotherapy Registry- Cardiovascular Toxicity

SIR-CVT is a non-interventional project with two primary objectives:

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

The study also addresses several secondary objectives:

- Identifying clinical, electrocardiographic, imaging, laboratory, and genetic markers for the early diagnosis of ICI-related myocarditis.

- Identifying markers for the early detection of other ICI-related adverse CV effects unrelated to myocarditis.

- Evaluating the relationship between previous chemotherapy regimens and ICI-related CV risk.

- Investigating the pathogenic mechanisms underlying myocarditis induced by immune checkpoint blockade (antiPD-L1/PD1 and anti-CTLA4).

- Assessing the impact of CV monitoring on patient quality of life and perceived quality of care.

The study involves of a baseline visit, after which patients are managed according to standard clinical protocols, including the frequency of follow-up visits. Participants will be followed until death, loss to follow-up, or the final visit 12 months after enrollment. All data collected will be used exclusively for research purposes.

As of February 2025, two patients have been enrolled and have undergone cardiac magnetic resonance and ultrasound imaging studies at the CNIC.

REACT: REVERSAL OF EARLY ATHEROSCLEROSIS THROUGH PERSONALIZED CURATIVE TREATMENT

Principal Investigator: *Borja Ibáñez*

REACT
Early Cure of Atherosclerosis

Atherosclerosis, the buildup of plaque in arteries, is the leading cause of cardiovascular diseases. This condition develops gradually as cholesterol, fat, blood cells, and other substances accumulate in the arterial walls, causing them to narrow and reducing blood flow to vital organs. Atherosclerosis contributes significantly to global morbidity and mortality, often beginning early in life and affecting multiple vascular systems.

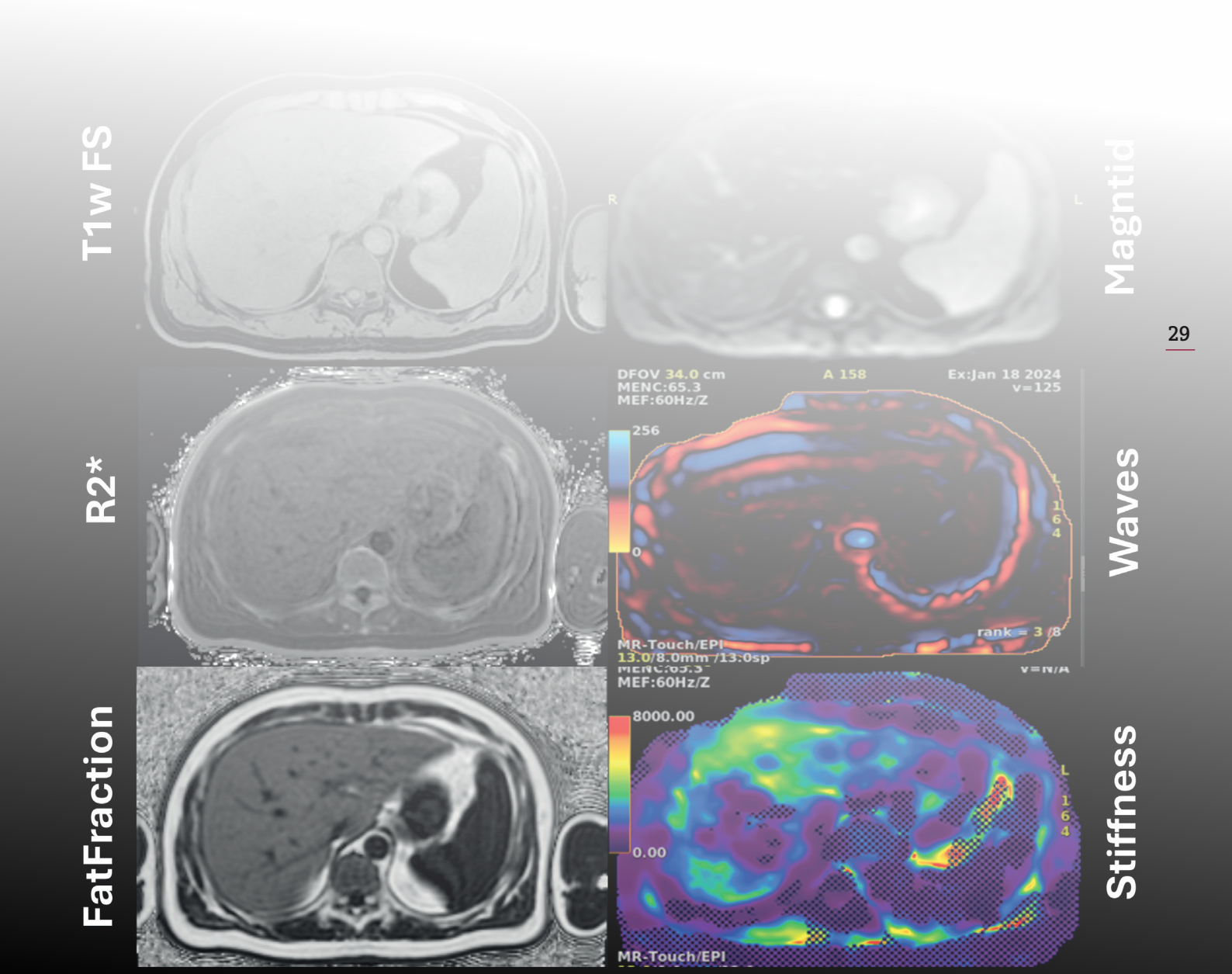
To address this major health challenge, the CNIC and the Rigshospitalet in Copenhagen have launched Phase 1 of the REACT project (Reversal of Early Atherosclerosis through Personalized Curative Treatment), funded by the Novo Nordisk Foundation. The primary goal of this phase is to determine the prevalence of asymptomatic (silent) atherosclerosis in a diverse, European-ancestry population across a wide age range (18–69 years). This will be achieved using advanced biomedical imaging techniques and circulating biomarkers, alongside traditional risk factors.

The REACT project focuses on early detection of atherosclerosis through a combination of imaging techniques, including vascular ultrasound (3DVUS), calcium scoring, and angiography, as well as biomarker analysis. The first phase is a prevalence study involving 16,000 participants (8,000 in Spain and 8,000 in Denmark). This study will provide a detailed understanding of how common asymptomatic atherosclerosis is at different ages and help develop a more precise risk evaluation algorithm than those currently in use.

The findings from Phase 1 will inform the design of Phase 2, a randomized clinical trial that will assess whether early

intervention—guided by imaging and including lifestyle changes, non-pharmacological approaches, and lipid-lowering treatments—can reduce atherosclerotic plaque burden or even lead to regression or cure.

The first participant was recruited on December 30, 2024, and the goal is to enroll all 8,000 participants within 18 months. This initiative will create a unique resource for future basic and clinical research.



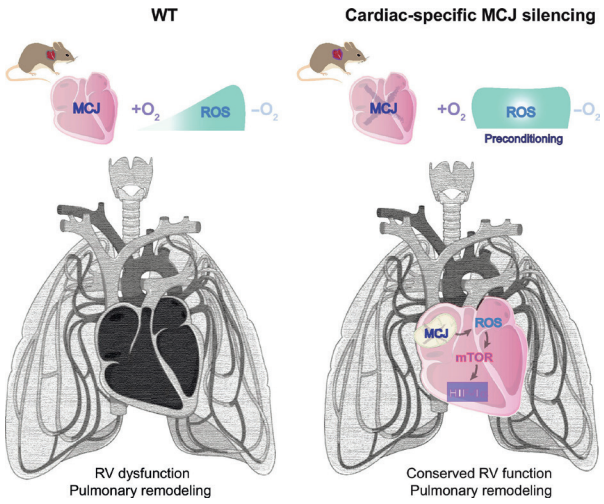
3 SCIENTIFIC HIGHLIGHTS BY PUBLICATION DATE

SCIENCE ADVANCES

FIRST THERAPEUTIC TARGET FOR PRESERVING HEART FUNCTION IN PATIENTS WITH PULMONARY HYPERTENSION

A CNIC team led by Dr. Guadalupe Sabio discovered a possible therapeutic target for pulmonary hypertension. The study, published in *Science Advances*, identified the first therapeutic target that can be modulated to preserve cardiac function in pulmonary hypertension, providing hope in the fight against this rare but fatal disease for which there is currently no cure.

The study was supported by grants from the Ministerio de Ciencia e Innovación (RED2022-134397-T, MINECO-PID2019-104399RB-I00, PGC2018-097019-B-I00), IMPACT-2021 PROJECT (PMP21/00057), Fundación Jesús Serra, the EFSD/Lilly European Diabetes Research Programme, Fundación BBVA, the Comunidad Autónoma de Madrid, and the Asociación Española Contra el Cáncer (AECC).



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CIRCULATION RESEARCH

APOE GENETIC VARIANTS LINKED TO ALZHEIMER DISEASE ARE ALSO ASSOCIATED WITH THE DEVELOPMENT OF SUBCLINICAL ATHEROSCLEROSIS

CNIC scientists found that one of the most potent genetic risk factors for Alzheimer's disease, apolipoprotein E4 (APOE4), is also associated with an increased risk of developing subclinical atherosclerosis in middle age. The study also demonstrated protection against subclinical atherosclerosis in people carrying the APOE2 variant, which protects against Alzheimer's disease.

The study received funding from the European Regional Development Fund (ERDF) and the European Social Fund (ESF).

The PESA study is funded jointly by the CNIC and Santander Bank. Additional financial support came from the ISCIII (PI15/02019, PI17/00590 & PI20/00819) and the BrightFocus Foundation. The present study involved the participation of investigators from the Spanish research networks for cardiovascular biomedicine (CIBERCV) and rare diseases (CIBERRER).

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NATURE CARDIOVASCULAR RESEARCH

NEW APPROACH TO THE DESIGN OF THERAPIES THAT ENHANCE THE EFFECT OF CHOLESTEROL-LOWERING DRUGS

A research team from the CNIC, in collaboration with Aarhus University in Denmark, uncovered a crucial mechanism that leads to the regression, or shrinkage, of atherosclerotic plaques. This discovery, published in ***Nature Cardiovascular Research***, highlights smooth muscle cell-derived cells in the arterial wall as a promising target for future therapies aimed at reducing plaque growth in advanced atherosclerosis.

The research was funded by the European Research Council (ERC 866240, JFB), the Ministerio de Ciencia e Innovación (PID2019-108568RB-I00, JFB), and the Novo Nordisk Foundation (NNF17OC0030688, JFB).

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CIRCULATION RESEARCH

NEW MECHANISM DISCOVERED FOR THE LIFE-THREATENING ARRHYTHMIAS IN ANDERSEN-TAWIL SYNDROME

A team at the CNIC led by Dr. José Jalife made a significant breakthrough in understanding the genetic basis of cardiac arrhythmias, particularly those related to Andersen-Tawil syndrome (ATS). The research, published in ***Circulation Research***, reveals how a specific genetic mutation (C122Y) in the Kir2.1 potassium channel not only disrupts the function of Kir2.1 itself but also impairs the main cardiac sodium channel, NaV1.5. This discovery establishes a direct link between the mutation and the life-threatening arrhythmias characteristic of ATS1.

The study was funded by the National Heart, Lung, and Blood Institute of the NIH (USA); Fundación "la Caixa"; Fundació La Marató de TV3; CIBERCV; the European Union Horizon 2020 Programme; and Program S2022/BMD7229 (Comunidad de Madrid). Imaging studies were performed at the TRIMA@CNIC node of the Distributed Biomedical Imaging Network (ICTS ReDIB).

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JACC: CARDIOONCOLOGY

CNIC SCIENTISTS IDENTIFY THERAPEUTIC TARGETS FOR THE PREVENTION OF HEART INJURY LINKED TO CANCER TREATMENT

CNIC scientists identified the mechanisms through which anthracyclines, a widely used class of anticancer drugs, damage the hearts of patients receiving this treatment. The study, published in ***JACC: CardioOncology***, also identified possible treatments for this complication, which affects an estimated one third of cancer survivors.

The study received support from the European Commission (ERC-CoG 819775 and H2020-HEALTH 945118), the Ministerio de Ciencia, Innovación y Universidades (PID2022-140176OB-I00), and the Comunidad Autónoma de Madrid through the Madrid Network for Nanomedicine in Molecular Imaging (P2022/BMD-7403 RENIM-CM).

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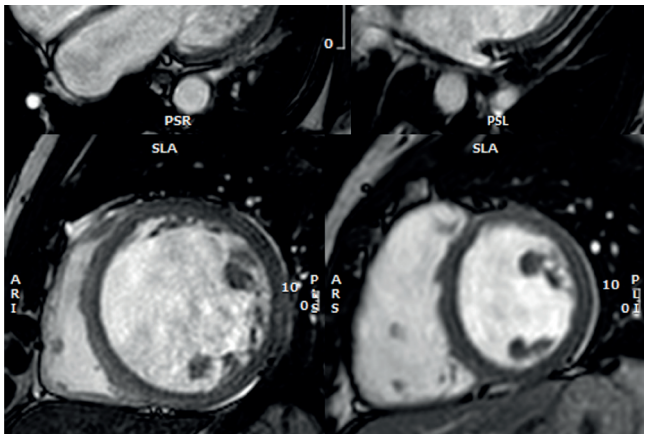
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

A NEW SPANISH STUDY PROVIDES THE FIRST STRATIFICATION OF THE RISK OF DILATED CARDIOMYOPATHY AMONG SYMPTOM-FREE GENETIC CARRIERS

Dilated cardiomyopathy is the leading cause of heart failure in young people and a major reason for heart transplants. This condition causes the heart to enlarge and lose its ability to effectively pump blood, putting patients at high risk of arrhythmias and sudden death. In 30%–40% of cases, the disease is linked to genetic mutations, and identifying these mutations allows doctors to screen family members for the altered gene.

The study was supported by the Sociedad Española de Cardiología (a Hereditary Cardiac Disease grant awarded in 2022) and the Instituto de Salud Carlos III through projects PI18/0004 and PI20/0320 (cofunded by the ERDF and the ESF).



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PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA

CNIC SCIENTISTS IDENTIFY THE KEY CELL TYPE FOR STRATEGIES TO PREVENT ATHEROSCLEROSIS IN PROGERIA SYNDROME

Hutchinson-Gilford progeria syndrome (HGPS) is an extremely rare genetic disease that causes accelerated aging, severe atherosclerosis, and premature death at an average age of 15 years. Despite the absence of typical cardiovascular risk factors, the leading cause of death in HGPS is premature atherosclerosis. The disease is caused by a mutation in the LMNA gene that leads to the production of progerin, a harmful version of the lamin A protein. The study demonstrated that premature atherosclerosis in a mouse model of HGPS is prevented by elimating progerin expression in arterial smooth muscle cells.

The study was funded by the Ministerio de Ciencia, Innovación y Universidades and the Agencia Estatal de Investigación (MICIU/AEI/10.13039/501100011033 and ERDF/EU (grants PID2022-141211OB-I00 and PID2022-137111OA-I00); the Comunidad Autónoma de Madrid (grants 2017-T1/BMD-5247 and 2021-5A/BMD-20944) cofinanced with European structural and investment funds; RYC2021-033805-I (MICIU/AEI/10.13039/501100011033 and European Union NextGenerationEU/PRTR); the Ministerio de Educación, Cultura y Deporte; Fundación "la Caixa"; and the Wellcome Trust.

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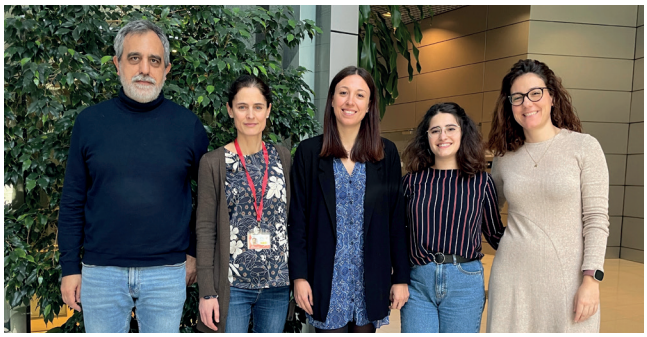
DEVELOPMENT CELL

A CNIC STUDY REVEALS THE KEY ROLE OF MITOCHONDRIAL PROTEINS IN CARDIAC REGENERATION

A study by the CNIC and the University of Bern revealed new insights into the role of mitochondria in heart regeneration. Published in ***Development Cell***, the research, led by Dr. José Antonio Enríquez and Dr. Nadia Mercader, identifies the cox7a protein family as crucial for the assembly of complex IV (CIV) in the mitochondrial respiratory chain, which is essential for cellular energy production.

The study was supported by the European Union Horizon 2020 programme (grants 874764 and 819717), the Human Frontier Science Program (grant RGP0016/2018), and the Swiss National Science Foundation (grant 320030E-164245).



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NUCLEIC ACIDS RESEARCH

A CNIC TEAM HAS CREATED AN INNOVATIVE TOOL FOR THE RELIABLE AND EFFICIENT STUDY OF GENE FUNCTION

A team from the CNIC, led by Rui Benedito, developed a new genetic tool called iSuRe-HadCre, which improves the precision and reliability of genetic alterations in tissues or individual cells. Published in ***Nucleic Acids Research***, this technology overcomes the limitations of the Cre-Lox system, which has been traditionally used for gene function analysis.

The study was funded by the Ministerio de Ciencia e Innovación, Fundación "la Caixa", the European Research Council, the Leducq Foundation, the Knut and Alice Wallenberg Foundation, and the Göran Gustafsson Foundation.

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JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

THE SOONER THE BETTER: TEACHING HEALTHY HABITS IN ELEMENTARY SCHOOL REDUCES ABDOMINAL FAT

A study led by the CNIC and the SHE Foundation, with support from Fundación "la Caixa", highlights the effectiveness of teaching healthy

habits in elementary schools as a way to prevent accumulation of abdominal fat. Published in ***The Journal of the American College of Cardiology***, the study is among the largest health promotion studies conducted in schools, with an extensive follow-up of participants.

Santos-Beneit G, Bodega P, de Cos-Gandoy A, de Miguel M, Rodríguez C, Orrit X, Carral V, Haro D, Carvajal I, Peyra C, Martínez-Gómez J, Fernández-Alvira JM, Fernández-Jiménez R, Fuster V. Effect of Time-Varying Exposure to School-Based Health Promotion on Adiposity in Childhood. J Am Coll Cardiol. 2024 Aug 6;84(6):499-508. doi: 10.1016/j.jacc.2024.04.065. PMID: 39084824.

JOURNAL OF CLINICAL INVESTIGATION

A NEW STUDY REVEALS A KEY MECHANISM DRIVING ATHEROSCLEROSIS IN HUTCHINSON-GILFORD PROGERIA SYNDROME

A team of researchers from the CNIC, CIB-CSIC, and ICMM-CSIC has made a significant breakthrough in understanding the mechanisms underlying atherosclerosis in Hutchinson-Gilford Progeria Syndrome (HGPS), a rare genetic disorder that accelerates aging. The study, published in ***The Journal of Clinical Investigation***, identifies abnormal activation of the YAP/TAZ pathway in endothelial cells as a key driver of atherosclerosis in HGPS patients.

The study was funded by grants from the Ministerio de Ciencia, Innovación y Universidades and the Agencia Estatal de Investigación (MICIU/AEI/10.13039/501100011033); FEDER/EU funds and the NextGenerationEU/PRTR (PID2022-141211OB-I00, PID2022-137111OA-I00, RYC2021-033805-I); and the Comunidad Autónoma de Madrid (grants 2017-T1/BMD-5247, 2021-5A/BMD-20944), with cofunding from the European Structural and Investment Fund.

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EUROPACE

A NEW IMAGE PROCESSING STRATEGY FOR CARDIAC MAGNETIC RESONANCE IMAGING IDENTIFIES CULPRIT AREAS UNDERLYING COMPLEX TACHYCARDIAS

A multicenter study published in ***Europace*** and led by investigators at Hospital Clínico San Carlos and the CNIC validated a new method that uses magnetic resonance imaging (MRI) to guide ablation procedures in patients with post-infarction ventricular tachycardias. The strategy precisely identifies the regions responsible for these arrhythmias in tissue affected by scarring after a myocardial infarction, thereby eliminating biases from manual parameter selection and allowing safer and more efficient planning.

The research was supported by the Ministerio de Ciencia e Innovación (MCIN/PID2019-109329RB-I00) and the Pro-CNIC Foundation, with additional support from the Sección de Arritmias de la Sociedad Española de Cardiología, the Fundación Interhospitalaria para la Investigación Cardiovascular, and the Eugenio Rodríguez Pascual Foundation.

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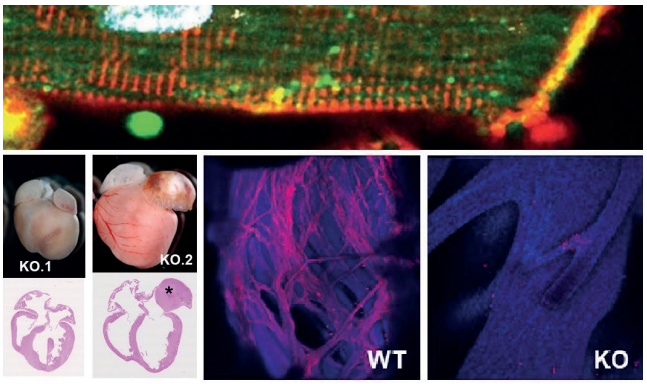
NATURE COMMUNICATIONS

KEY MECHANISM DISCOVERED IN THE DEVELOPMENT AND FUNCTIONING OF THE CARDIAC CONDUCTION SYSTEM

A study published in ***Nature Communications*** by a team of researchers from the Rare Diseases Research Institute of the Instituto de Salud Carlos III (ISCIII), CIBER, the CNIC, Universitat Pompeu Fabra (UPF), and the Severo Ochoa Molecular Biology Center (CBM, CSIC-UAM) identified the protein Dhx36 as an essential regulator of heart development and function, particularly in the cardiac conduction system.

The study, led by scientists Pablo Gómez del Arco (ISCIII), Pura Muñoz-Cánoves (UPF and Altos Labs), and Juan Miguel Redondo (CBM, CSIC-UAM), demonstrates that Dhx36 modulates gene networks controlling cardiomyocyte differentiation by resolving G-quadruplex structures in the promoters of key genes in the cardiac conduction system. This function is critical for the formation of specialized cells that make up the conduction system, which transmits and regulates the heart's electrical impulses.



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JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

PROGRESSION OF SUBCLINICAL ATHEROSCLEROSIS PREDICTS ALL-CAUSE MORTALITY RISK

A study led by Dr. Valentín Fuster at Mount Sinai Fuster Heart Hospital and the CNIC demonstrates that atherosclerosis burden and progression in asymptomatic individuals are independently associated with all-cause mortality. Published in ***The Journal of the American College of Cardiology***, the study highlights the value of quantifying carotid and coronary atherosclerosis using advanced imaging technology to predict overall mortality.

Fuster V, García-Álvarez A, Devesa A, Mass V, Owen R, Quesada A, Fuster JJ, García-Lunar I, Pocock S, Sánchez-González J, Sartori S, Peyra C, Andrés V, Muntendam P, Ibáñez B. Influence of Subclinical Atherosclerosis Burden and Progression on Mortality. J Am Coll Cardiol. 2024 Oct 8;84(15):1391-1403. doi: 10.1016/j.jacc.2024.06.045. PMID: 39357937.

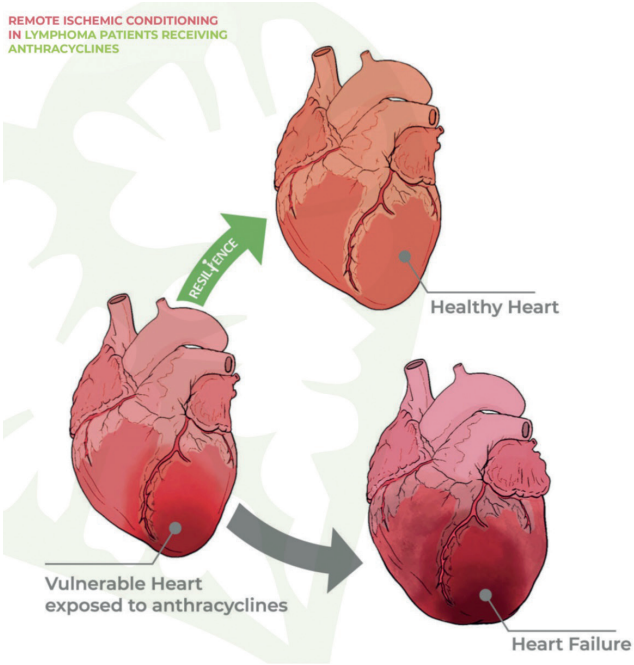
EUROPEAN JOURNAL OF HEART FAILURE

THE RESILIENCE TRIAL: PREVENTING HEART INJURY CAUSED BY ANTICANCER DRUGS

The RESILIENCE clinical trial investigates the safety and effectiveness of remote ischemic conditioning in preventing cardiac injury caused by anthracycline chemotherapy in lymphoma patients. This innovative multinational double-blind project, funded by the European Union, aims to reduce the incidence of chronic heart failure in cancer survivors and improve their quality of life.

Coordinated by the CNIC and supported by the European Society of Cardiology and Philips Healthcare, among other partners, RESILIENCE aims to validate innovative methods to protect patients at high risk of cancer therapy-related cardiac dysfunction, offering new therapeutic perspectives for a significant medical challenge.

The RESILIENCE trial is funded by the European Commission (H2020-HEALTH, grant number 945118).



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JACC: CLINICAL ELECTROPHYSIOLOGY

GENETICS COULD EXPLAIN A LARGE NUMBER OF YOUNG ADULTS WITH PACEMAKERS WITHOUT AN IDENTIFIED CAUSE

A study led by CNIC cardiologists Juan Pablo Ochoa and Pablo García-Pavía, published in ***JACC Clinical Electrophysiology***, revealed that rare genetic variants increase the risk of cardiac conduction disorders in young adults requiring a pacemaker. According to the study, 15% of patients have a direct genetic mutation, while an additional 30% show relevant genetic alterations. This highlights the importance of genetics in the diagnosis and management of these disorders.

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NATURE MEDICINE AND EUROPEAN HEART JOURNAL

CNIC SCIENTISTS DISCOVER A NEW CARDIOVASCULAR RISK FACTOR AND IDENTIFY A DRUG ABLE TO REDUCE ITS EFFECTS

A study by researchers at the CNIC, published in ***Nature Medicine***, establishes clonal hematopoiesis—caused by acquired mutations in blood stem cells—as a direct risk factor for atherosclerosis, a condition underlying most cardiovascular diseases. Previously, it was unclear whether clonal hematopoiesis was a cause or consequence of cardiovascular disease. A second CNIC study, published in the ***European Heart Journal***, suggests that colchicine, an ancient anti-inflammatory medication, could be used to mitigate the effects of TET2-related clonal hematopoiesis.

These findings, presented at the European Society of Cardiology meeting, pave the way for personalized treatments targeting this newly confirmed risk factor for cardiovascular disease.

The PESA study is funded jointly by the CNIC and Santander Bank. The two studies were additionally funded by the Ministerio de Ciencia, Innovación y Universidades (PLEC2021-008194), CIBERCV, Fundación "la Caixa" (LCF/PR/HR17/52150007; LCF/PR/HR22/52420011), and Fundació La Marató de TV3 (202314-31).

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CIRCULATION

A NEW MECHANISM OF EARLY-ONSET ATHEROSCLEROSIS IN A PREMATURE AGING SYNDROME

A CNIC study, led by Drs. Vicente Andrés and Magda Hamczyk and published in ***Circulation***, identifies endothelial-to-mesenchymal transition (EndMT) as a key mechanism in premature atherosclerosis and a potential therapeutic target. EndMT involves pathological changes in endothelial cells, such as increased immune cell recruitment and LDL permeability, which accelerate the formation of atherosclerotic plaques.

The study focuses on progeria, a genetic disease that causes early-onset atherosclerosis and premature death. Researchers found that the TGFβ1-SMAD3 pathway, central to EndMT, is hyperactivated in mouse models of progeria, while its inhibition with the drug SIS3 improves vascular symptoms.

The study was funded by the Ministerio de Ciencia, Innovación y Universidades and the Agencia Estatal de Investigación (MICIU/AEI/10.13039/501100011033) and the ERDF/EU (PID2022-141211OB-I00).

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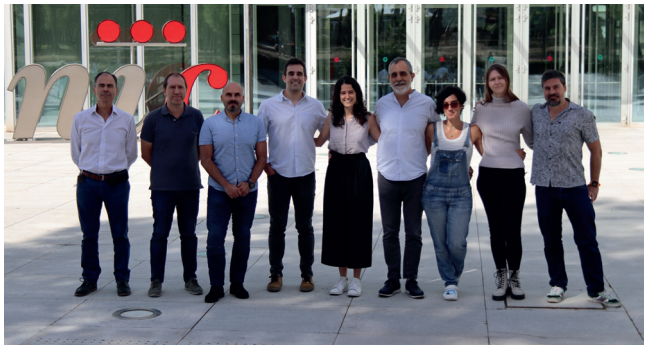
CELL

SCIENTISTS AT THE CNIC DISCOVER AN UNEXPECTED INVOLVEMENT OF SODIUM TRANSPORT IN MITOCHONDRIAL ENERGY GENERATION

The GENOXPHOS group from the CNIC and CIBERFES, led by Dr. José Antonio Enríquez, has uncovered an essential role of sodium in cellular energy production. The study, published in ***Cell***, reveals that mitochondrial complex I not only transports protons, as proposed by the chemiosmotic theory of 1961, but also exchanges sodium ions, creating a gradient critical for efficient production of ATP, the primary carrier of cellular energy. This discovery sheds light on the molecular mechanism behind Leber's Hereditary Optic Neuropathy (LHON), a neurodegenerative disease caused by mitochondrial DNA defects. Dysfunction in sodium-proton transport by complex I leads to cell death, triggering this pathology.

The study was supported by the Ministerio de Ciencia e Innovación (MCIN/RTI2018-099357-B-I00), CIBERFES (CB16/10/00282), the Human Frontier Science Program (grant RGP0016/2018), and Leducq Transatlantic Networks (17CVD04).



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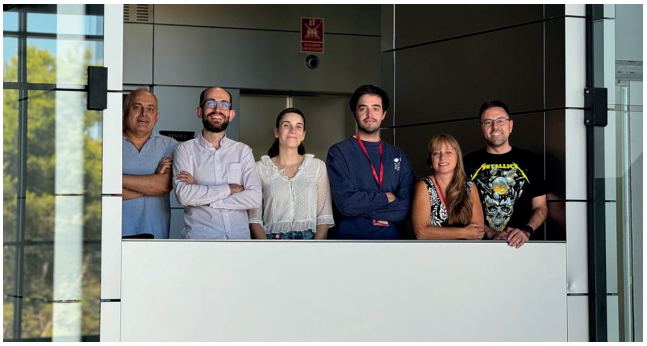
SCIENCE ADVANCES

A NEW CNIC STUDY REVEALS HOW CELLS RESPOND TO MECHANICAL SIGNALS FROM THEIR ENVIRONMENT

A study conducted at the CNIC, led by Dr. Jorge Alegre-Cebollada, has revealed the fundamental role of tissue viscoelasticity—a largely unexplored property—in cellular function. The extracellular matrix (ECM), a network of proteins that supports and connects cells, influences processes such as cell migration, proliferation, and differentiation through its mechanical properties, including stiffness and viscoelasticity.

The study was made possible thanks to funding from the Ministerio de Ciencia, Innovación y Unoversidades, the European Research Council, and the Comunidad Autónoma de Madrid through the interdisciplinary consortium Tec4Bio-CM. The study included core contributions from four Tec4Bio-CM principal investigators, at the CNIC, ICMM-CSIC, and Polytechnic University of Madrid.



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NATURE COMMUNICATIONS

CNIC SCIENTISTS DISCOVER A KEY MECHANISM IN FAT CELLS THAT PROTECTS THE BODY AGAINST ENERGETIC EXCESS

A team from the CNIC led by Professor Miguel Ángel del Pozo Barriuso has identified a key mechanism in fat cells that allows them to safely expand and store energy, preventing tissue damage. The study, published in ***Nature Communications***, could pave the way for new therapies for metabolic diseases such as obesity and lipodystrophy.

The study was funded by Ministerio de Ciencia, Innovación y Universidades and the Agencia Estatal de Investigación with cofunding from the ERDF (MICIU/AEI/SAF2017-83130-R, IGP-SO grant MINSEV1512-07-2016, BFU2016-81912-REDC, and SAF2020 [PID2020-118658RB-I00]), Fundación "la Caixa" (AtheroConvergence, HR20-00075), the Comunidad Autónoma de Madrid (Tec4Bio-CM, S2018/...), Fundació La Marató de TV3 (201936-30-31), and the AECC (PROYE20089DELP).

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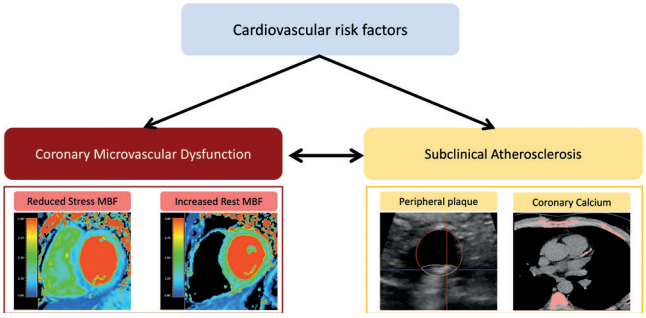
JACC: CARDIOVASCULAR IMAGING

CARDIOMETABOLIC RISK FACTORS IN APPARENTLY HEALTHY INDIVIDUALS ARE LINKED TO ALTERED CORONARY MICROCIRCULATION

A CNIC study, published in ***JACC: Cardiovascular Imaging***, examines how cardiometabolic risk factors and subclinical atherosclerosis impact coronary microvascular function in asymptomatic middle-aged individuals. Microvascular function, essential for regulating blood flow and oxygen supply to the heart, was assessed using magnetic resonance imaging in 453 participants of the PESA-CNIC-Santander study.

The PESA study is funded jointly by the CNIC and Banco Santander. Additional support was provided by the European Commission (ERC-CoG 819775 and H2020-HEALTH 945118), the Ministerio de Ciencia, Innovación y Universidades (PID2019-110369RB-I00), and the Madrid Network of Nanomedicine in Molecular Imaging- Comunidad Autónoma de Madrid (S2017/BMD-3867 RENIM-CM).



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NATURE METHODS

CNIC PRESENTS IFLPMOSAICS, AN INNOVATIVE GENETIC TOOLKIT FOR THE STUDY OF GENE FUNCTION

A team from the CNIC led by Dr. Rui Benedito has developed iFlpMosaics, an innovative set of genetic tools and mouse lines that enhances the study of gene function and its implications in health

and disease. The study, published in ***Nature Methods***, presents a groundbreaking approach that overcomes the limitations of current methods for generating genetic mosaics, enabling more precise investigation of the effects of somatic mutations on cellular biology and diseases.

This study was funded by the European Research Council through Starting Grant AngioGenesHD (638028) and Consolidator Grant AngioUnrestUHD (101001814), the Ministerio de Ciencia e Innovación (SAF2017-89299-P and PID2020-120252RB-I00), and Fundación "la Caixa" (HR19-00120 and HR22-00316 AngioHeart).

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4 CNIC NEWS AND VIEWS

1. VISITING SCIENTISTS AT THE CNIC

SPAIN'S GROWING INTERNATIONAL PROFILE IN SCIENTIFIC RESEARCH MAKES IT AN INCREASINGLY ATTRACTIVE DESTINATION FOR VISITING SCIENTISTS FROM ALL OVER THE WORLD.

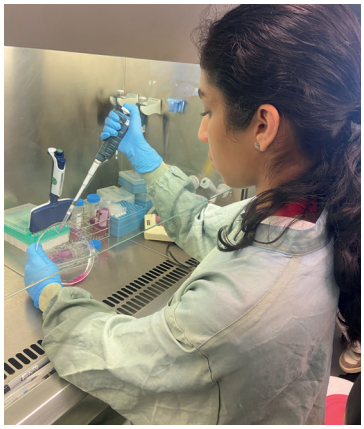
FOUNDATION OCCIDENT VISITING RESEARCHERS PROGRAM

The Jesús Fundación Occident and the CNIC have worked together since 2013 to bring visiting scientists to the CNIC within the framework of a Visiting Researchers program.

The Program supports visits by international scientists to Spanish research centers, with the aim of building strong inter-institutional bonds and promoting new lines of research.

On May 10, 2024, the CNIC and Fundación Occident held a scientific event as part of this Program. The event showcased preliminary research results from Dr. Mark Hlatky (Stanford University) and Dr. Carlos Morillo (Calgary University), current participants in the groups of Drs. Borja Ibáñez and Inés García Lunar and Drs. José Jalife and David Filgueiras, respectively. Representatives from both organizations, including CNIC leadership and research hosts, participated in the event, reinforcing their ongoing partnership.

EU CONTEST FOR YOUNG SCIENTISTS



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

The 2023 winner, student Sachi N. Premaratne, from Sweden, was the recipient of the ***CNIC Recognition*** for her project "Antibodies targeting transient receptor potential vanilloid 1 as potential drug candidates for the treatment of chronic pain". She visited the CNIC in July 2024 to learn about the center's projects directly from our researchers. The awardee learnt also about the infrastructure and technology available at the center and how these are used to address and solve the challenges of cardiovascular health research.

The 2024 winner, Ludmila Kvasnovska, from Slovakia, with the project "Potential biomarkers of age-related chronic inflammation", will complete her visit to the center in 2025.

These visits are financed with CNIC Severo Ochoa Grant CEX2020-001041-S.

2-AWARDS AND HONORS

DR. VALENTÍN FUSTER, CNIC'S GENERAL DIRECTOR RECEIVED IN 2024 THE FOLLOWING PRESTIGIOUS AWARDS:

- **The AstraZeneca Foundation Honorific Award for Excellence in Scientific Research**

The AstraZeneca Foundation gave its Honorific Award for Excellence in Scientific Research of the VII Young Researcher Awards to Valentín Fuster, for his outstanding career as a researcher in the field of cardiology.

- **The International Atherosclerosis Society Award**

The International Atherosclerosis Society awarded Dr. Valentín Fuster, the Antonio M. Gotto Jr. Prize in Atherosclerosis Research in recognition of his outstanding contributions to the understanding and treatment of atherosclerosis. The award was presented by Peter Libby, President of the International Atherosclerosis Society, during the opening ceremony of the International Atherosclerosis Society's Annual Symposium in Oman.

This award honors Dr. Fuster's outstanding contributions to the understanding of the progression, prevention, and treatment of atherosclerosis, also known as hardening of the arteries.

- **Lifetime Achievement Award of the World Heart Federation (WHF)**

The WHF presented Dr. Valentín Fuster with its Lifetime Achievement Award 2024. The award acknowledges his notable contributions in the field of cardiovascular disease and his particular devotion to combating this disease around the world. The prestigious award recognises the international leadership Dr. Fuster has displayed over the last four decades and his ground-breaking contributions to cardiovascular medicine, both in the field of research and from the clinical perspective and, more recently as champion of cardiovascular health worldwide.

- **The Medal of the European Society for Clinical Investigation**

The European Society for Clinical Investigation (ESCI) awarded the Albert Struyveberg Medal to Dr. Valentín Fuster. With this prize the ESCI acknowledges Dr. Fuster's valuable contribution to cardiology worldwide.

DR. JOSÉ JALIFE NAMED DOCTOR HONORIS CAUSA IN SCIENCES BY THE UPSTATE MEDICAL UNIVERSITY OF SYRACUSE

Dr José Jalife, Group Leader of Heart Arrhythmias was named Doctor Honoris Causa by the State University of New York, Upstate Medical University of Syracuse, NY (USA).

DR. HÉCTOR BUENO RECEIVES THE ESC PRESIDENT'S AWARDS 2024 AT THE CONGRESS OF THE EUROPEAN SOCIETY OF CARDIOLOGY

Dr. Héctor Bueno, principal investigator of the Multidisciplinary Translational Cardiovascular Research group at CNIC, Coordinator of the Clinical Hospitalization Area and Research of the Cardiology Service at the 12 de Octubre Hospital, leader of the i+12 Multidisciplinary Translational Cardiovascular Research Institute, has received the ESC President's Awards 2024 from the European Society of Cardiology (ESC) at the ESC Congress 2024 in London. This award recognizes Héctor Bueno's outstanding individual contribution to the ESC. According to Prof. Franz Weidinger, President of the ESC, Dr. Bueno´s years of selfless service to ESC have made "a profound impact in many ways, to members of the ESC but also for our patients".

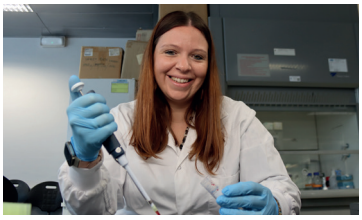
DR. MARÍA ÁNGELES MORO JOINS THE ROYAL NATIONAL ACADEMY OF PHARMACY

Dr. María Ángeles Moro Sánchez, principal investigator of the Neurovascular Pathophysiology at CNIC, has been appointed as a Full Member of the Royal National Academy of Pharmacy. During her Inaugural Lecture, she emphasized her commitment to the institution's objectives: promoting scientific knowledge in health, advancing research in innovative treatments, and fostering continuous education for healthcare professionals.

DR. RODRIGO FERNÁNDEZ JIMÉNEZ RECEIVES THE GABRIELLA MORREALE NATIONAL YOUTH RESEARCH AWARD

The CNIC principal investigator Rodrigo Fernández Jiménez (Cardiovascular Health and Imaging Group) received the Gabriella Morreale National Youth Research Award in the area of Medicine and Health Sciences. The National Research Awards recognise the merit of researchers with Spanish nationality who perform outstanding work in scientific fields of international importance, and who make a significant contribution to the advance of scientific knowledge and the progress of humankind.

DR. CINTIA FOLGUEIRA COBOS RECEIVES THE RISING STAR AWARD 2024



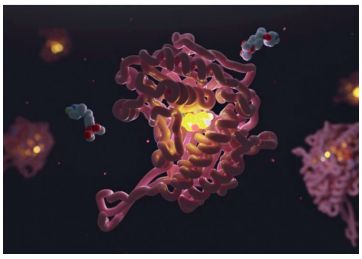
The European Foundation for the Study of Diabetes (EFST) Rising Star 2024 awarded the CNIC postdoctoral researcher, Dr Cintia Folgueira Cobos a grant of 30.000 euros.

DR. GUIOMAR MENDIETA RECEIVES A JACC REWARDS FOR A PESA-CNIC-SANTANDER STUDY

The researcher Guiomar Mendieta (former Cardiojoven fellow) received in 2024, the 2023 William W Parmley Young Author Achievement Award for her work "Determinants of Progression and Regression of Subclinical Atherosclerosis over 6 Years", which was published in the Journal of the American College of Cardiology (JACC) in November 2023 and was led by Drs. Valentín Fuster and Borja Ibáñez. The William W Parmley award, in honor of Dr William W Parmley, ex-editor in chief of the JACC, rewards papers published in the JACC whose principal authors are completing their sub-specialization in cardiology and/or are doctoral candidates.

CNIC RECEIVES A DONATION TO INVESTIGATE HUTCHINSON–GILFORD PROGERIA SYNDROME

The Molecular and Genetic Cardiovascular Pathophysiology Laboratory headed by Dr Vicente Andrés at CNIC received a donation of 11,060 euros from the Alexandra Peraut Progeria Association for its research project into the Hutchinson–Gilford progeria syndrome (HGPS), an ultra-rare genetic disease that affects 1 in every 20 million people.



CNIC STUDY NAMED NATURE PJ IMAGING ARTICLE OF THE YEAR FOR 2024

A study coordinated by Dr. Carlos Pérez Medina, principal investigator of the Nanomedicine and Molecular Imaging Group at CNIC, has been named by the journal npj Imaging as its Article of the Year for 2024 (npj Imaging). The article, 'Macrophage PET imaging in mouse models of cardiovascular disease and cancer with an apolipoprotein-inspired radiotracer', describes an innovative probe for the noninvasive detection of macrophages—immune cells that play a key role in the inflammatory response—by positron emission tomography (PET). The study, published in May 2024, was carried out by scientists at the CNIC and Mount Sinai Hospital in New York.

3- SCIENTIFIC EVENTS

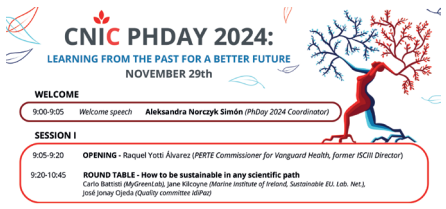
CNIC CONFERENCE ON CARDIOVASCULAR RISK FACTORS AND BRAIN HEALTH, JUNE 3-5, 2024

The first 2024 CNIC Conference highlighted strong links between cardiovascular health and cognitive decline, especially in diseases like Alzheimer's. Experts emphasized that vascular damage can contribute to or precede brain degeneration, and that early intervention offers a chance to prevent dementia. The conference called for better integration of cardiovascular and brain research, stressing the importance of controlling cardiovascular risk factors to protect brain health. This conference was co-sponsored by the International Society for Cerebral Blood Flow and Metabolism.

CNIC CONFERENCE ON UNDERSTANDING IMMUNITY IN CARDIOVASCULAR DISEASE, NOVEMBER 13-15, 2024

The second 2024 CNIC Conference highlighted the critical role of the immune system in cardiovascular health and disease. Experts in immunology, vascular biology, and cardiology discussed how immune cell dysregulation contributes to conditions such as atherosclerosis, heart failure, and inflammatory cardiomyopathies. The event emphasized that both exaggerated inflammatory and autoimmune responses can cause long-term cardiac damage. Advances in immunotherapy offer promising new treatment approaches. Key topics included immune regulation in heart repair, cardiovascular inflammation, autoimmunity, and immune cell interactions in heart disease.

CNIC PhDAY 2024: "LEARNING FROM THE PAST FOR A BETTER FUTURE"



The CNIC PhDay is an open forum for undergraduate and graduate students, lab technicians and postdoctoral researchers to develop their careers as scientists, exchange new ideas and network. Every year, more than 200 people gather at the CNIC to share experiences and generate new ideas and collaborations.

The 10th edition of CNIC PhDay was held on November 29, 2024, organized by doctoral students and postdoctoral researchers. Under the theme "Learning from the Past for a Better Future," the event focused on the impact of science on the environment and society.

The event focused into the role and impact of science on the environment and society. Invited experts from different scientific fields and perspectives gave thought-provoking presentations and discussions. The focus was on the conscious use of available resources, deepening the understanding of the intricate relationship between research workflows, biotechnology, public health and the environment.

4- OUTREACH ACTIVITIES

INTERNATIONAL WOMEN'S DAY 2024 @ CNIC

CNIC held a symposium on the 8th of March to highlight the inspirational example of our female researchers. The event "Women scientists from around the world at CNIC" was held with the participation of five female international researchers who conduct their investigative work at our Center: Valeria Caiolfa, Italy; Beatrice Oluwatayo, Nigeria; Gillian Dunphy, United Kingdom; Jyothi K C, India and Henar Cuervo, Spain. The researchers talked to the attendees about aspects such as what a career in science is like for women abroad, the differences between countries and cultures, maternity during a career in research and their research at CNIC among other topics.

INTERNATIONAL DAY OF WOMEN AND GIRLS IN SCIENCE AT CNIC

In Spain, only 16% of STEM professionals are women. On the International Day of Women and Girls in Science, we prepared an activity to attempt to encourage vocation by examples of real women who work at CNIC.

The event took place on 15 February in the CNIC auditorium.

First of all, high scool attendads watched the video showing the experience of 4 women from the CNIC who are part of the PESA HEALTH CNIC-Santander project. This video is part of the #EmpresasQueInspiran initiative of the Bertelsmann Foundation to help awaken vocations in the field of science and technology. Those attending were able to learn about their experience, as well as the talent and profiles needed to work on such an interesting scientific challenges.

This was followed by a colloquium entitled 'Women and Girls in Science' and finally they were able to learn about the CNIC's training Plan and its flagship programme: ACÉRCATE.

WORLD HEART DAY

- **Dr. Borja Ibáñez: Now is the Best Time to Start Taking Care of Ourselves**

On September 29, World Heart Day (#WorldHeartDay), the CNIC's Scientific Director, Dr. Borja Ibáñez, explained to the general public what atherosclerosis is, how studies such as PESA-CNIC-SANTANDER and REACT contribute to its prevention, and at what age we should begin taking steps to prevent it, among other important topics.

- **Dr. Ana García and Dr. Nadia Mercader: Heart attack in women and how a heart attack regenerates**

Two CNIC researchers take part in the journal Saber Vivir magazine, on the occasion of World Heart Day, presented by Dr. Valentín Fuster, Director General of the CNIC and Director of the Mount Sinai Fuster Heart Hospital in New York.

Women are now much more aware that the risk of suffering a heart attack is similar to that of men. Dr. Ana García Álvarez, principal investigator of the Heart Failure and Pulmonary Hypertension translational research Group at CNIC and head of the Cardiology Department at the Hospital Clínic in Barcelona, considers this new perception to be 'a great step forward because it promotes self-care'. Although she insists that 'there is still a long way to go'.

Dr. Ana García Álvarez explains the reasons and the way in which heart attacks occur in women. She also stresses the importance of seeing a doctor as soon as possible: 'It takes about 6 hours from the onset of a heart attack until there is irreversible damage, but it is advisable to go to the doctor much earlier'.

Dr. Nadia Mercader, visiting professor at the CNIC and professor at the University of Bern (Switzerland), discussed the possibility of heart regeneration after a heart attack: "We know that all cells in the body contain the same (or very similar) genetic information because they are copies of another cell that has divided before. It may be possible that heart cells can redivide and recover the organ after a heart attack. But there is still a lot of research to be done.".

- **European Researchers' Night 2024 at CNIC**

Through eight activities open to both adults and children, attendees of the 15th European Researchers' Night in Madrid, hosted by CNIC, participated in seminars and workshops that brought them closer to the research conducted at the Center. This event offers an exciting opportunity to dive into the world of science and innovation. From fascinating experiments to inspiring talks, CNIC provides a glimpse into the latest discoveries and technological wonders.

- **CNIC at the 2024 Science Week**

From November 7 to 15, CNIC organized 11 activities during the 24th Science and Innovation Week, welcoming participants of all ages. Attendees engaged in practical workshops and had the chance to visit CNIC's state-of-the-art laboratories.

El CNIC recibe apoyo del Instituto de Salud Carlos III (ISCIII), del Ministerio de Ciencia, Innovación y Universidades (MICIU) y es un Centro de Excelencia Severo Ochoa. Esta actividad es parte de la ayuda CEX2020-001041-S financiada por el MICIU/AEI/10.13039/501100011033.

5- OTHER ACTIVITIES

CNIC PARTICIPATES IN THE FORO TRANSFIERE, THE MAIN MEETING ON SCIENCE, TECHNOLOGY AND INNOVATION IN THE SOUTH OF EUROPE

CNIC participated in the 13th European Meeting on Science Technology and Innovation. Known as Foro Transfiere, this is the main meeting for R+D in the south of Europe and its aim is to share scientific and technological knowledge, promote innovation, connect science and business, and facilitate the transfer of knowledge so that scientific and technological developments reach people's daily lives. The Foro Transfiere is co-organized by the Ministry of Science and Innovation, the Andalusian Regional Government and Malaga City Council.

6- SOCIAL AND CNIC

CNIC JOINS THE 2024 HEART RACE

CNIC took part in the 15th Popular Heart Race organized by Spanish Heart Foundation, promoting cardiovascular health and fitness through community participation.

CNIC ADVANCES EQUALITY: COLLECTIVE AGREEMENT NEGOTIATION, EQUALITY DISTINCTION RECOGNITION, AND NEW PLANS FOR EQUALITY AND HARASSMENT PREVENTION

CNIC begins negotiating its first collective agreement, the agreements reached will benefit the more than 400 professionals working at the Center. This is a major milestone for the Center's staff.

Moreover, CNIC was awarded in 2025 with the Equality in Business Distinction from the Ministry of Equality and is negotiating a new Equality Plan and a new Protocol for the Prevention of Harassment.

5 TRAINING PROGRAMS

Training is one of the CNIC's core activities, and the Center has devised a comprehensive training plan, the CNIC-Joven Training Plan that 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 the personal goal of Valentín Fuster "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 with a unique opportunity to immerse themselves in the world of biomedical research. Through a rigorous national selection process, the program seeks to ignite and nurture their passion for pursuing a career in biomedical science.

Over the course of one week at 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 2024: 8

4º ESO – CNIC

The Madrid Directorate General of Secondary Education launched the 4th Year ESO + Company Program in the 2008-2009 academic year. This program, classified as a complementary activity, is being adopted voluntarily by an increasing number of schools. Its aim is to bridge the gap between the educational system and the labor market by providing educational placements in companies and institutions. This initiative helps young people become better prepared to make informed decisions about their academic and professional futures, motivating them and equipping them with essential skills.

The CNIC collaborates with the 4ºESO-CNIC Program every year. In 2024, 21 science students from fourteen schools spent four full days at the CNIC laboratories exploring possible 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 2024: 35

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 2024, 12 students from the following universities began internships at the CNIC related to their final degree thesis dissertation (TFG) under the guidance of a CNIC supervisor:

- 7 students from the Autonomous University of Madrid
- 3 students from the Complutense University of Madrid
- 1 student from the University Alcalá de Henares
- 1 student from the University Carlos III of Madrid

In 2024, an additional 18 students from both Spanish and international universities participated in various types of university internships at the CNIC under the mentorship of a CNIC supervisor. This group included seven students from Spanish universities, seven Erasmus students from universities in Amsterdam, Prague, Hannover, and Twente, and four other international students from universities in Edinburgh, London, Mahidol, and Vienna.

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 students studying for a master's degree at a Spanish university to carry out their experimental project (TFM) in a CNIC laboratory.

Fellowships in 2024: 11

Other Master's Student Internships

In 2024, another 18 students from the following universities began to work on their TFM under the guidance of a CNIC supervisor:

- 7 students from the Autonomous University of Madrid
- 3 students from the Complutense University of Madrid
- 2 students from the Polytechnic University of Madrid
- 1 student from the University of Valencia
- 1 student from the University of Amsterdam, the Netherlands
- 1 student from Vrije Universiteit Amsterdam, the Netherlands
- 1 student from Università degli Studi di Firenze Scienze della Salute Umana, Italy
- 1 student from Hannover Medical School

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 quality of 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 2024: 113

- Graduate students at the CNIC awarded a PhD degree in 2024: 23
- Enrolled at the Autonomous University of Madrid: 19
- Enrolled at the Complutense University of Madrid: 2
- Enrolled at the Polytechnic University of Madrid: 1
- Enrolled at the University Carlos III of Madrid: 1

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 of 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.

Attendants 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 2024: 22

PROGRAMS FOR RESIDENT MEDICAL INTERNS

RES@CNIC SEC PROGRAM

The Res@CNIC-SEC Program (in 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 participating in RES@CNIC 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 2024: 25 from the following hospitals:

- Complejo Asistencial Universitario de León
- Complejo Hospitalario Universitaria A Coruña
- Hospital Clínic de Barcelona
- Hospital de la Santa Creu i Sant Pau
- Hospital Universitario Central de Asturias
- Hospital Universitario Clínico San Carlos
- Hospital Universitario Cruces

Hospital Universitario de La Princesa

Hospital Universitario Fundación Jiménez Díaz

Hospital Universitario La Paz

Hospital Universitario Ramón y Cajal

Hospital Universitario Virgen de las nieves Granada

Hospital Universitario Virgen del Rocío

INVESMIR SEC PROGRAM

The INVESMIR SEC Program offers resident medical interns the opportunity during their specialization period to further 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 2024 one resident cardiologist intern from Hospital Universitario Joan XXIII (Tarragona) participated in this Program.

PROGRAMS FOR RESEARCHERS

COFUND CURE HEART AND BRAIN POSTDOCTORAL PROGRAM

The Cure Heart & Brain postdoctoral COFUND program, led by CNIC, invites outstanding researchers of any nationality to conduct cutting-edge research on the heart, the brain, and their interconnection—topics of critical medical and social significance.

The selection and recruitment process adheres 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.

Fellows have the freedom to select their host research group at CNIC and choose from a variety of secondment options. Applicants may propose their own research topics, provided these align with the Center's objectives and can be feasibly executed within CNIC's infrastructure.

The Cure Heart & Brain program collaborates with 24 Associated Partners worldwide, representing diverse sectors. These partners enhance the program's translational scope by offering secondment opportunities and specialized training.

In 2024, four postdoctoral researchers joined CNIC through the program's first call. In 2025, the remaining eight positions will be filled from applicants to the second call.

Cure Heart & Brain cnic postdoctoral fellowship programme

More info: www.cnic.es

Co-funded by the European Union

CARDIO JOVEN PROGRAM

The aim of this Program (also organized in collaboration with the SEC) is to foster high-quality translational research in the cardiovascular area in Spanish National Health System centers through training programs providing theory and practical training for cardiologists with a research vocation. One trainee is selected every two years year.

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).

The program is aimed at cardiologists who aspire to carry out advanced clinical and research work at any center within the Spanish National Health System.

b) International training. The Program offers a period of training toward a Master's Degree at the London School of Hygiene and Tropical Medicine (90 ECTS)

VALENTÍN FUSTER PROGRAM

The VALENTÍN FUSTER Program was established with the aim of:

Developing a profile of a translational cardiovascular researcher capable of bridging the gap between research and clinical practice by applying research-generated knowledge to patient care and generating research hypotheses from clinical practice.

Supporting the integration of research as a key component of the medical career path within the National Health System.

This program, in collaboration with the 12 de Octubre Hospital Research Institute (i+12), facilitates the incorporation of a translational research physician specializing in cardiovascular fields at the 12 de Octubre University Hospital (H12O) through a five-year contract.

PRACTICAL TRAINING FOR TECHNICAL SCHOOL STUDENTS

In 2024, the program welcomed 15 technical school students specializing in "Pathological Anatomy and Cytodiagnostics," "Clinical and Biomedical Laboratory," and "Cell Culture" to gain hands-on experience in CNIC's laboratories during a three-month training period.

The CNIC maintains collaborative agreements with 19 technical training institutions to support these internships. Each center submits a single candidate, and the host research groups select participants from among the nominations.

Additionally, the CNIC collaborates with the two DUAL Centers in Madrid offering biomedicine-related programs: Instituto de Educación Secundaria Moratalaz, specializing in "Clinical and Biomedical Laboratory," and Instituto de Educación Secundaria San Juan de la Cruz, focusing on "Diagnostic Imaging and Nuclear Medicine." In September 2024, four students from these DUAL Centers began their nine-month practical training 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 Sociedad Española de Cardiología (SEC). The course is aimed at R3, R4, and R5 residents in cardiology and other specialties related to cardiovascular disease, and translational researchers working in the field of cardiology.

Participants receive 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 XVI edition of this course was held in the SEC Auditorium on December 12, 2024.

6 FACTS AND FIGURES
SCIENTIFIC PUBLICATIONS 2024

PUBLICATIONS INDEXED IN WoS IN JOURNALS WITH AN IMPACT FACTOR

	NUMBER	PERCENTAGE
ARTICLES	256	65%
REVIEWS	29	7%
OTHER	110	28%
TOTAL	**395**	

PUBLICATIONS IN TOP JOURNALS

130 (33%)

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

59 (15%)

A)

JOURNAL'S QUALITY	NUMBER	PERCENTAGE
D1	194	49%
Q1	319	81%
Q2	58	15%
Q3	13	3%
Q4	5	1%

B)

OPEN ACCESS	NUMBER	PERCENTAGE
ALL TYPES OF OPEN ACCESS	251	64%
GOLD OPEN ACCESS	227	57%

C)

LEADERSHIP	NUMBER	PERCENTAGE
FIRST, LAST OR CORRESPONDING AUTHOR	218	55%

D)

AFFILIATION AND COLLABORATION	NUMBER	PERCENTAGE
INTERNATIONAL COLLABORATION	233	59%
NATIONAL COLLABORATION	162	41%

E)

OTHER IMPACT INDICATORS	NUMBER	PERCENTAGE
DOCS CITED	196	50%
HIGHLY CITED PAPERS*	10	3%
HOT PAPERS**	4	1%

European Heart Journal

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

nature neuroscience

Science

Cell

Circulation Research

Circulation

nature medicine

The NEW ENGLAND JOURNAL of MEDICINE

Filter Summary:
Dataset: Web of Science
Domestic/International Collaboration: All
Time Period: [2024, 2024]
Include Early Access documents: true
Document Type: [All types of documents]
Organization Name: [Centro Nacional de Investigaciones Cardiovasculares (CNIC)]
Exported date: 21/01/2025

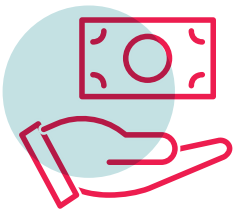
**Highly Cited Papers: Articles that have received enough citations to be ranked in the top 1% in their respective scientific areas, type of document and year of publication.*

***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 2024 Publications at
https://www.cnic.es/es/investigacion/publicaciones/resultados?y=2024

COMPETITIVE FUNDING*

GRANTS STARTING 2024



NATIONAL
76 GRANTS
€ 18,585,819

INTERNATIONAL
14 GRANTS
€ 12,657,024

INCLUDING:
1 HORIZON-ERC-ADG
1 HORIZON-ERC-POC
1 HORIZON-EIC-PATHFINDEROPEN
1 HORIZON-MSCA-COFUND
5 ERA4HEALTH-CARDINNOV

OTHER GRANTS ACTIVE IN 2024

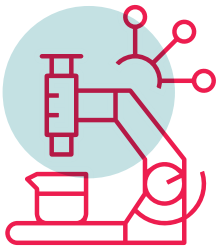
NATIONAL
248 GRANTS
€ 57,450,243

INCLUDING:
SEVERO OCHOA AWARD FOR THE PERIOD 2022-2025

INTERNATIONAL
40 GRANTS
€ 28,837,514

INCLUDING:
5 ERC-CONSOLIDATOR
5 H2020 HEALTH NEWORKS, 2 OF THEM COORDINATED BY CNIC
3 LEDUCQ FOUNTATION NETWORKS
2 ERA NETS AND EU4HEALTH
1 NIH
1 BRIGHT FOCUS FOUNDATION GRANT
1 NOVONORDISK
1 HORIZON-EIC-ATHFINDERCHALLENGES

TECHNOLOGY TRANSFER*



23 ACTIVE PATENT FAMILIES
08 LICENSED INVENTIONS
05 NEW PATENT FAMILIES, INCLUDING 03 PRIORITY FILINGS
71 NEW MATERIAL TRANSFER AGREEMENTS
12 NEW CONFIDENTIAL DISCLOSURE AGREEMENTS
03 NEW RESEARCH COLLABORATION AGREEMENTS

DATA AS OF 31/12/2024

HUMAN RESOURCES*

SCIENTIFIC AND TECHNICAL STAFF 430

WOMEN

269	161

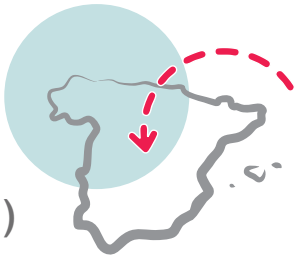
MEN

GROUP LEADERS 32

MEN

23	9

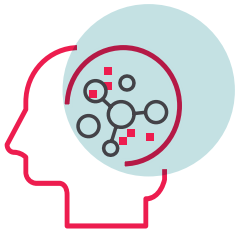
WOMEN



48 (11%)

SCIENTIFIC AND TECHNICAL STAFF FROM OUTSIDE SPAIN

(19 COUNTRIES)



CARDIOLOGIST GROUP LEADERS 11

MEN

7	4

WOMEN

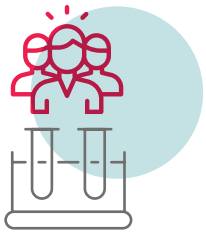
VISITING SCIENTISTS 262

WOMEN

158	104

MEN

(34 FROM INSTITUTIONS OUTSIDE SPAIN; 13 COUNTRIES)



HEADS OF TECHNICAL UNITS 11

WOMEN

6	5

MEN

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