3 SCIENTIFIC HIGHLIGHTS
BY PUBLICATION DATE

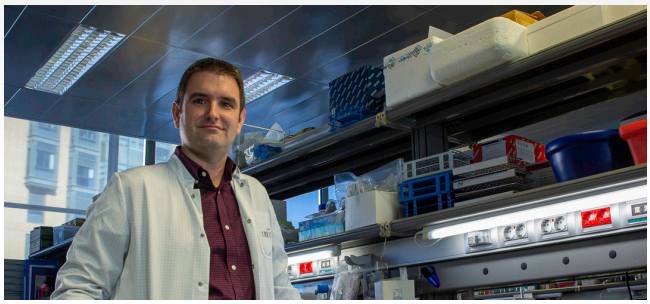
NATURE CNIC SCIENTISTS DISCOVER A CELL BEHAVIOR PATTERN THAT PREDICTS CARDIOVASCULAR DISEASE

Scientists led by Dr. Andrés Hidalgo at the CNIC have discovered that circulating neutrophils acquire different behavior patterns during inflammatory processes. The study, published in Nature, identifies a harmful neutrophil behavior associated with cardiovascular disease.

Crainiciuc G, Palomino-Segura M, Molina-Moreno M, Sicilia J, Aragones DG, Li JLY, Madurga R, Adrover JM, Aroca-Crevillén A, Martin-Salamanca S, Del Valle AS, Castillo SD, Welch HCE, Soehnlein O, Graupera M, Sánchez-Cabo F, Zarbock A, Smithgall TE, Di Pilato M, Mempel TR, Tharaux PL, González SF, Ayuso-Sacido A, Ng LG, Calvo GF, González-Díaz I, Díaz-de-María F, Hidalgo A. Behavioural immune landscapes of inflammation. Nature. 2022 Jan;601(7893):415-421. https://doi.org/10.1038/s41586-021-04263-y

NATURE CARDIOVASCULAR RESEARCH MUTATIONS ACQUIRED BY BLOOD CELLS ARE AN INDICATOR OF CARDIOVASCULAR RISK

Scientists at the CNIC and Columbia University, New York have published a review article in Nature Cardiovascular Research examining the role of acquired mutations linked to clonal hematopoiesis in cardiovascular disease.



Tall AR, Fuster JJ. Clonal hematopoiesis in cardiovascular disease and therapeutic implications. Nat Cardiovasc Res. 2022 Feb;1(2):116-124. https://doi.org/10.1038/s44161-021-00015-3

NATURE COMMUNICATIONS CNIC SCIENTISTS IDENTIFY A SHUTTLE PROTEIN REQUIRED FOR THE NUCLEAR IMPORT OF PROTEINS ESSENTIAL FOR ORGAN GROWTH AND DEVELOPMENT

Organ growth and regeneration require the entry into the cell nucleus of proteins that activate essential genes for these processes. This process is the subject of a new study by CNIC scientists, led by Dr. Miguel Ángel del Pozo, who heads the Mechanoadaptation and Caveolae Biology group, and group member Dr. Asier Echarri. The scientists have identified the mechanism that controls the nuclear import of these proteins in response to mechanical stimuli, such as the hemodynamic forces generated by arterial blood flow, tumor rigidity, or locomotory movements during routine activities like walking or sports.

García-García M, Sánchez-Perales S, Jarabo P, Calvo E, Huyton T, Fu L, Ng SC, Sotodosos-Alonso L, Vázquez J, Casas-Tintó S, Görlich D, Echarri A, Del Pozo MA. Mechanical control of nuclear import by Importin-7 is regulated by its dominant cargo YAP. Nat Commun. 2022 Mar 4;13(1):1174. https://doi.org/10.1038/s41467-022-28693-y

CIRCULATION

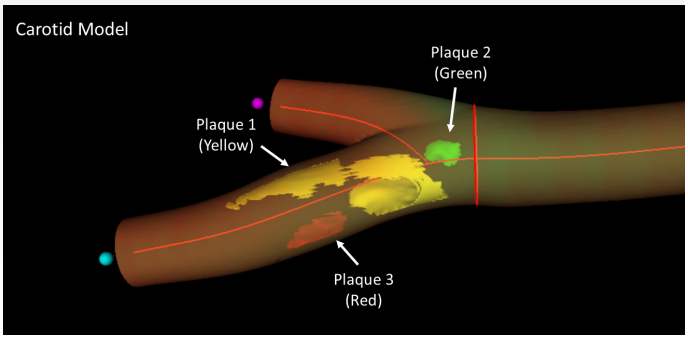
A CNIC STUDY HIGHLIGHTS THE RISKS OF MITOCHONDRIAL THERAPEUTIC INTERVENTIONS

Research carried out at the CNIC has demonstrated that mixing mitochondrial DNAs (mtDNAs) of different origins can have damaging effects over the medium and long term. mtDNA is a component of the genetic material that is transmitted exclusively from mothers to their children.

Lechuga-Vieco AV, Latorre-Pellicer A, Calvo E, Torroja C, Pellico J, Acín-Pérez R, García-Gil ML, Santos A, Bagwan N, Bonzon-Kulichenko E, Magni R, Benito M, Justo-Méndez R, Simon AK, Sánchez-Cabo F, Vázquez J, Ruíz-Cabello J, Enríquez JA. Heteroplasmy of Wild-Type Mitochondrial DNA Variants in Mice Causes Metabolic Heart Disease With Pulmonary Hypertension and Frailty. Circulation. 2022 Apr 5;145(14):1084-1101. https://doi.org/10.1161/CIRCULATIONAHA.121.056286

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY: CARDIOVASCULAR IMAGING

3D MATRIX ULTRASOUND ACCURATELY IDENTIFIES CARDIOVASCULAR INJURY IN HEALTHY INDIVIDUALS



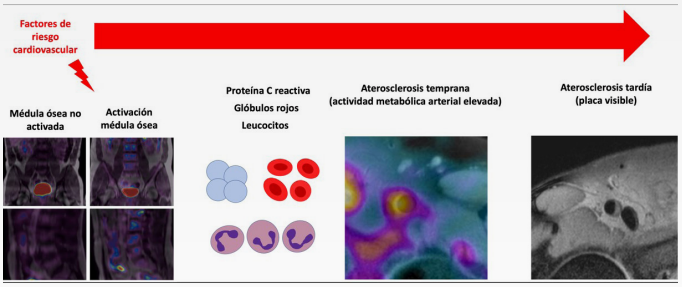
A new imaging technique for real 3D vascular ultrasound could become a key tool in strategies aimed at preventing cardiovascular disease in apparently healthy persons, complementing traditional risk parameters such as cholesterol and high blood pressure. The new results, published in JACC: Cardiovascular Imaging, show that real 3D vascular ultrasound is reliable, accurate, and faster than previous methods for the assessment of plaque volume in the carotid and femoral arteries.

López-Melgar B, Mass V, Nogales P, Sánchez-González J, Entrekin R, Collet-Billon A, Rossello X, Fernández-Friera L, Fernández-Ortiz A, Sanz J, Bentzon JF, Bueno H, Ibáñez B, Fuster V. New 3-Dimensional Volumetric Ultrasound Method for Accurate Quantification of Atherosclerotic Plaque Volume. JACC Cardiovasc Imaging. 2022 Jun;15(6):1124-1135. https://doi.org/10.1016/j.jcmg.2022.01.005

EUROPEAN HEART JOURNAL

BONE MARROW CONTRIBUTES TO THE DEVELOPMENT OF ATHEROSCLEROSIS

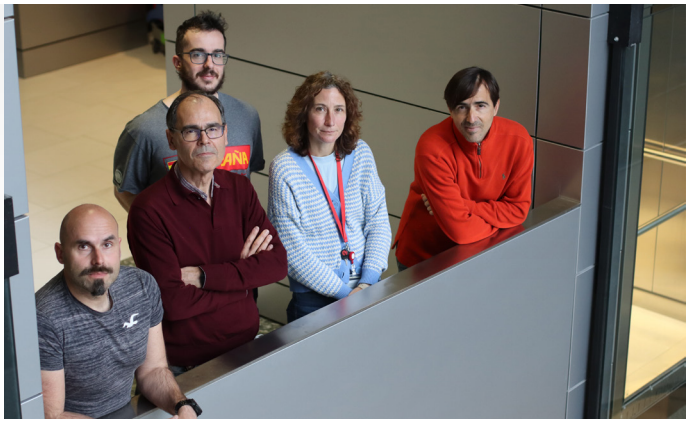
The activation of the bone marrow appears to play a key role in the origin and development of atherosclerosis, the pathological process underlying cardiovascular conditions such as myocardial infarction and stroke. A study carried out by scientists at the CNIC and led by cardiologists Drs. Valentín Fuster and Borja Ibáñez suggests that the bone marrow is activated in response to known cardiovascular risk factors. In the study, published in the European Heart Journal, the researchers show that these risk factors lead to an increase in the number of circulating inflammatory cells, which go on to trigger the initiation and subsequent progression of atherosclerotic disease.



Devesa A, Lobo-González M, Martínez-Milla J, Oliva B, García-Lunar I, Mastrangelo A, España S, Sanz J, Mendiguren JM, Bueno H, Fuster JJ, Andrés V, Fernández-Ortiz A, Sancho D, Fernández-Friera L, Sanchez-Gonzalez J, Rossello X, Ibanez B, Fuster V. Bone marrow activation in response to metabolic syndrome and early atherosclerosis. Eur Heart J. 2022 May 14;43(19):1809-1828. https://doi.org/10.1093/eurheartj/ehac102

eBIOMEDICINE

SCIENTISTS DISCOVER A NEW METHOD FOR THE EARLY DETECTION OF SUBCLINICAL ATHEROSCLEROSIS



A study published in the journal eBioMedicine identifies new biomarkers that predict the presence of subclinical atherosclerosis. The study was carried out by scientists from the Spanish Cardiovascular Research Network (CIBERCV) working at the CNIC and the Instituto de Investigación Sanitaria-Fundación Jiménez Díaz-Universidad Autónoma de Madrid (IIS-FJD-UAM), in partnership with other institutions.

Núñez E, Fuster V, Gómez-Serrano M, Valdivielso JM, Fernández-Alvira JM, Martínez-López D, Rodríguez JM, Bonzon-Kulichenko E, Calvo E, Alfayate A, Bermudez-Lopez M, Escola-Gil JC, Fernández-Friera L, Cerro-Pardo I, Mendiguren JM, Sánchez-Cabo F, Sanz J, Ordovás JM, Blanco-Colio LM, García-Ruiz JM, Ibáñez B, Lara-Pezzi E, Fernández-Ortiz A, Martín-Ventura JL, Vázquez J. Unbiased plasma proteomics discovery of biomarkers for improved detection of subclinical atherosclerosis. EBioMedicine. 2022 Feb;76:103874. https://doi.org/10.1016/j.ebiom.2022.103874

REDOX BIOLOGY

CNIC SCIENTISTS DISCOVER A NEW MECHANISM INVOLVED IN THE MODULATION OF HEART MUSCLE ELASTICITY

Scientists at the CNIC, in collaboration with an international scientific team, have described a new mechanism of modulation of the mechanical properties of the heart, based on the oxidation of the protein titin, which is the main protein responsible for the passive elasticity of the heart muscle.

Herrero-Galán E, Martínez-Martín I, Sánchez-González C, Vicente N, Bonzón-Kulichenko E, Calvo E, Suay-Corredera C, Pricolo MR, Fernández-Trasancos Á, Velázquez-Carreras D, Careaga CB, Abdellatif M, Sedej S, Rainer PP, Giganti D, Pérez-Jiménez R, Vázquez J, Alegre-Cebollada J. Basal oxidation of conserved cysteines modulates cardiac titin stiffness and dynamics. Redox Biol. 2022 Jun;52:102306. https://doi.org/10.1016/j.redox.2022.102306

NATURE CARDIOVASCULAR RESEARCH

A CNIC TEAM CREATES A DYNAMIC 3D ATLAS OF THE FORMATION OF THE EMBRYONIC HEART

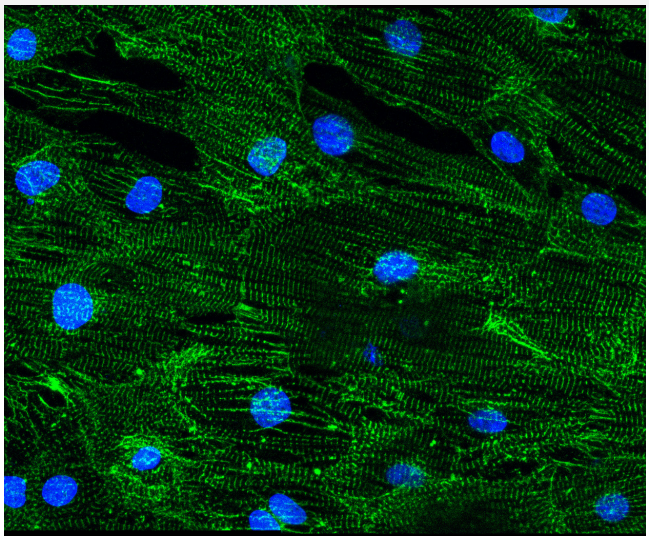
Scientists at the CNIC have used a collection of mouse tissue samples to create a 3D atlas of the formation of the heart during embryonic and fetal development. The 3D atlas has allowed the scientists to identify the first appearance of left–right asymmetry in the heart. The study, published today in Nature Cardiovascular Research, provides important information on the development of congenital heart malformations.

Esteban I, Schmidt P, Desgrange A, Raiola M, Temiño S, Meilhac SM, Kobbelt L, Torres M. Pseudodynamic analysis of heart tube formation in the mouse reveals strong regional variability and early left–right asymmetry. Nat Cardiovasc Res. 2022 May;1: 504-517. https://doi.org/10.1038/s44161-022-00065-1

ELIFE

STUDY REVEALS HOW DUCHENNE MUSCULAR DYSTROPHY CAUSES HEART RHYTHM PROBLEMS

Abnormalities in the proteins responsible for transmitting electrical signals in the heart likely cause abnormal heart rhythms in patients with Duchenne muscular dystrophy (DMD), shows a study published in eLife.

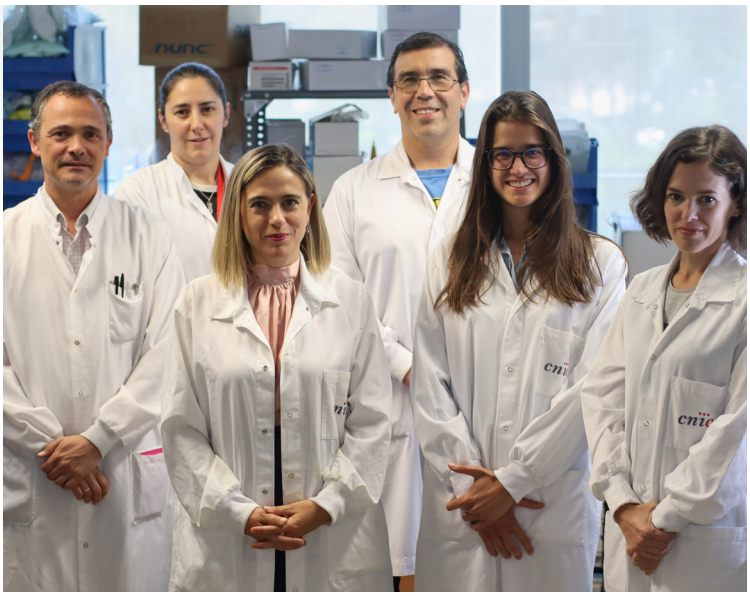


Jimenez-Vazquez EN, Arad M, Macías Á, Vera-Pedrosa ML, Cruz FM, Gutierrez LK, Cuttita AJ, Monteiro da Rocha A, Herron TJ, Ponce-Balbuena D, Guerrero-Serna G, Binah O, Michele DE, Jalife J. SNTA1 gene rescues ion channel function and is antiarrhythmic in cardiomyocytes derived from induced pluripotent stem cells from muscular dystrophy patients. Elife. 2022 Jun 28;11:e76576. https://doi.org/10.7554/eLife.76576

HEPATOLOGY

IMMUNE CELLS IN THE LIVER REGULATE BODY TEMPERATURE

A study published in Hepatology demonstrates that the activation of thermogenesis in the livers of obese mice contributes to weight loss and improves diabetes symptoms.



Crespo M, Nikolic I, Mora A, Rodríguez E, Leiva-Vega L, Pintor-Chocano A, Horrillo D, Hernández-Cosido L, Torres JL, Novoa E, Nogueiras R, Medina-Gómez G, Marcos M, Leiva M, Sabio G. Myeloid p38 activation maintains macrophage-liver crosstalk and BAT thermogenesis through IL-12-FGF21 axis. Hepatology. Epub 2022. Hepatology. 2023 Mar 1;77(3):874-887. https://doi.org/10.1002/hep.32581

EUROPEAN JOURNAL OF HEART FAILURE

SPANISH SCIENTISTS COMBINE GENETIC AND IMAGING DATA TO IMPROVE THE TREATMENT OF DILATED CARDIOMYOPATHY

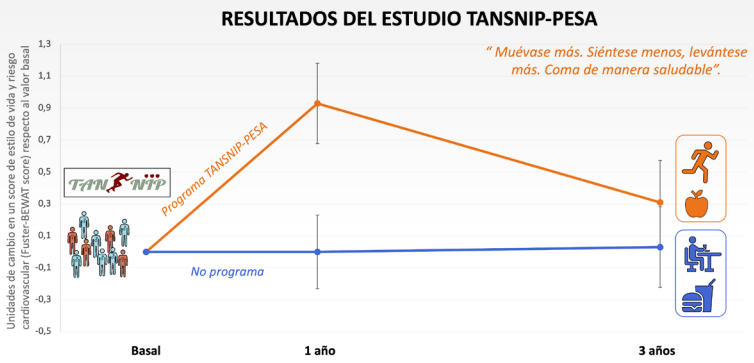
Combining a person's genetic profile with imaging data obtained by cardiac magnetic resonance accurately predicts the prognosis of patients with dilated cardiomyopathy, the most frequent cause of heart failure.

Mirelis JG, Escobar-Lopez L, Ochoa JP, Espinosa MÁ, Villacorta E, Navarro M, Casas G, Mora-Ayestarán N, Barriales-Villa R, Mogollón-Jiménez MV, García-Pinilla JM, García-Granja PE, Climent V, Palomino-Doza J, García-Álvarez A, Álvarez-Barredo M, Cabrera-Borrego E, Ripoll-Vera T, Peña-Peña ML, Rodríguez-González E, Gallego-Delgado M, Gonzalez-Carrillo J, Fernández-Ávila A, Rodríguez-Palomares JF, Brugada R, Bayes-Genis A, Dominguez F, García-Pavía P. Combination of late gadolinium enhancement and genotype improves prediction of prognosis in non-ischaemic dilated cardiomyopathy. Eur J Heart Fail. 2022 Jul;24(7):1183-1196. https://doi.org/10.1002/ejhf.2514

EUROPEAN HEART JOURNAL

ONE CHANGE A DAY MAKES 365 CHANGES IN A YEAR

Many cardiovascular disorders can be prevented by taking action to reduce risk factors. Making even small behavioral changes and sticking with them over the long term can help to preserve cardiovascular health. This is the conclusion of a study conducted at the CNIC and published in the European Heart Journal. The study also demonstrates that the workplace is an ideal setting for programs promoting the adoption of heart-healthy habits and producing major health benefits.



Garcia-Lunar I, van der Ploeg HP, Fernández Alvira JM, van Nassau F, Castellano Vázquez JM, van der Beek AJ, Rossello X, Fernández-Ortiz A, Coffeng J, van Dongen JM, Mendiguren JM, Ibáñez B, van Mechelen W, Fuster V. Effects of a comprehensive lifestyle intervention on cardiovascular health: the TANSNIP-PESA trial. Eur Heart J. 2022 Oct 11;43(38):3732-3745. https://doi.org/10.1093/eurheartj/ehac378

ELIFE

CNIC SCIENTISTS UNCOVER OPPOSING ROLES OF P38 PROTEINS IN CARDIAC HYPERTROPHY

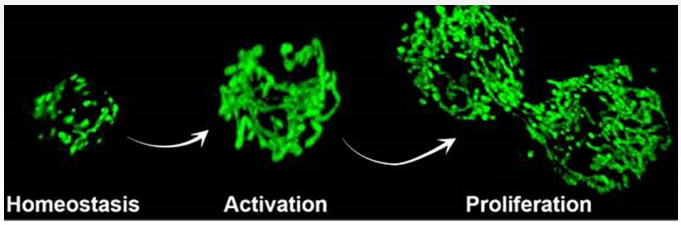
A study carried out by scientists at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) and led by Dr. Guadalupe Sabio has identified a key role for the MKK3/6–p38γ/δ signaling pathway in the development of cardiac hypertrophy. The results, published in the journal eLife, suggest that inhibition of p38γ/δ could be a useful therapeutic strategy for diseases such as hypertrophic cardiomyopathy; however, this avenue remains unexplored because of the lack of specific inhibitors

for these kinase enzymes. The study also shows the opposite effect upon inhibition of another member of this protein family, p38α, indicating that long-term clinical use of p38α inhibitors to treat chronic disease risks damage to the heart.

Romero-Becerra R, Mora A, Manieri E, Nikolic I, Santamans AM, Montalvo-Romeral V, Cruz FM, Rodríguez E, León M, Leiva-Vega L, Sanz L, Bondía V, Filgueiras-Rama D, Jiménez-Borreguero LJ, Jalife J, Gonzalez-Teran B, Sabio G. MKK6 deficiency promotes cardiac dysfunction through MKK3-p38γ/δ-mTOR hyperactivation. Elife. 2022 Aug 16;11:e75250. https://doi.org/10.7554/eLife.75250

CELL STEM CELL

RESEARCHERS AT CNIC, UPF, ICREA, CIBERNED AND CIBERFES IDENTIFY A MECHANISM THAT MAINTAINS MITOCHONDRIA FUNCTION IN MUSCLE STEM CELLS AND THAT CAN BE STIMULATED IN OLD AGE

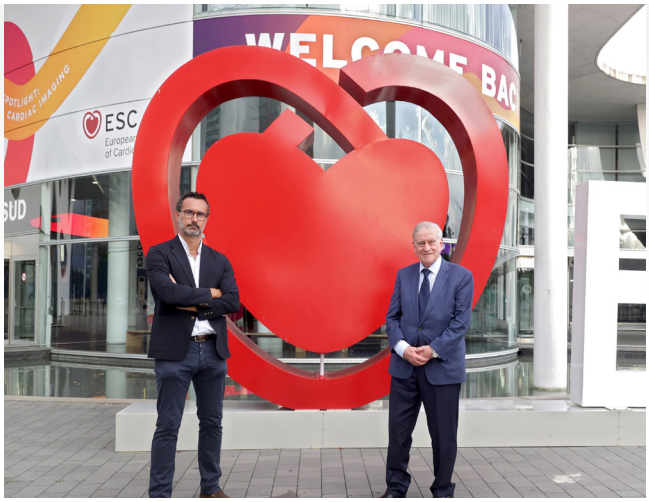


Researchers at the Centro Nacional de Investigaciones Cardiovasculares (CNIC), Universidad Pompeu Fabra, ICREA, Centro de Investigación Biomédica de Enfermedades Neurodegenerativas (CIBERNED) and Centro de Investigación Biomédica en Red Fragilidad y Envejecimiento Saludable (CIBERFES) have identified a physiological mechanism that sustains the regenerative capacity of muscle stem cells, and that fails at old age. This failure can be overcome genetically and pharmacologically, hence restoring old stem cell regenerative functions.

Hong X, Isern J, Campanario S, Perdiguero E, Ramírez-Pardo I, Segalés J, Hernansanz-Agustín P, Curtabbi A, Deryagin O, Pollán A, González-Reyes JA, Villalba JM, Sandri M, Serrano AL, Enríquez JA, Muñoz-Cánoves P. Mitochondrial dynamics maintain muscle stem cell regenerative competence throughout adult life by regulating metabolism and mitophagy. Cell Stem Cell. 2022 Sep 1;29(9):1298-1314.e10. https://doi.org/10.1016/j.stem.2022.07.009

THE NEW ENGLAND JOURNAL OF MEDICINE

THE POLYPILL REDUCES CARDIOVASCULAR MORTALITY BY 33% IN PATIENTS TREATED AFTER MYOCARDIAL INFARCTION



The polypill developed by the Centro Nacional de Investigaciones Cardiovasculares (CNIC) and Ferrer, which includes three drugs (aspirin, an angiotensin-converting enzyme (ACE) inhibitor, and a statin), is effective at preventing secondary adverse cardiovascular events in people who have previously had a heart attack. The polypill reduces mortality from cardiovascular causes in this population by 33%.

Castellano JM, Pocock SJ, Bhatt DL, Quesada AJ, Owen R, Fernandez-Ortiz A, Sanchez PL, Marin Ortuño F, Vazquez Rodriguez JM, Domingo-Fernández A, Lozano I, Roncaglioni MC, Baviera M, Foresta A, Ojeda-Fernandez L, Colivicchi F, Di Fusco SA, Doehner W, Meyer A, Schiele F, Ecarnot F, Linhart A, Lubanda JC, Barczi G, Merkely B, Ponikowski P, Kasprzak M, Fernandez Alvira JM, Andres V, Bueno H, Collier T, Van de Werf F, Perel P, Rodriguez-Manero M, Alonso Garcia A, Proietti M, Schoos MM, Simon T, Fernandez Ferro J, Lopez N, Beghi E, Bejot Y, Vivas D, Cordero A, Ibañez B, Fuster V; SECURE Investigators. Polypill Strategy in Secondary Cardiovascular Prevention. N Engl J Med. 2022 Sep 15;387(11):967-977. https://doi.org/10.1056/NEJMoa2208275

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

SCIENTISTS AT THE CNIC AND HOSPITAL PUERTA DE HIERRO DEVELOP A TOOL TO DETERMINE IF DILATED CARDIOMYOPATHY HAS A GENETIC ORIGIN

Scientists at the CNIC and Hospital Universitario Puerta de Hierro Majadahonda have developed a software application that predicts the likelihood that a case of dilated cardiomyopathy is caused by a genetic mutation. The research was carried out in collaboration with hospitals in Spain, Italy, and the Netherlands. The findings, published in the Journal of the American College of Cardiology (JACC), will allow physicians to adjust the treatment of dilated cardiomyopathy patients appropriately and to identify family members who have also inherited the disease. The software application is available online at www.madriddcmscore.com.

Escobar-Lopez L, Ochoa JP, Royuela A, Verdonschot JAJ, Dal Ferro M, Espinosa MA, Sabater-Molina M, Gallego-Delgado M, Larrañaga-Moreira JM, Garcia-Pinilla JM, Basurte-Elorz MT, Rodríguez-Palomares JF, Climent V, Bermudez-Jimenez FJ, Mogollón-Jiménez MV, Lopez J, Peña-Peña ML, Garcia-Alvarez A, López-Abel B, Ripoll-Vera T, Palomino-Doza J, Bayes-Genis A, Brugada R, Idiazabal U, Mirelis JG, Dominguez F, Henkens MTHM, Krapels IPC, Brunner HG, Paldino A, Zaffalon D, Mestroni L, Sinagra G, Heymans SRB, Merlo M, Garcia-Pavia P. Clinical Risk Score to Predict Pathogenic Genotypes in Patients With Dilated Cardiomyopathy. J Am Coll Cardiol. 2022 Sep 20;80(12):1115-1126. https://doi.org/10.1016/j.jacc.2022.06.040

CELLULAR AND MOLECULAR LIFE SCIENCES

NEW MECHANISM LINKING INFLAMMATION AND PATHOLOGIC CARDIOVASCULAR REMODELING

The immune-inflammatory response contributes to the pathological remodeling of arteries in various cardiovascular diseases. Research published in CMLS has shed new light on one of the mechanisms linking the immune-inflammatory response to vascular disease by describing the key role played by the early lymphocyte activation antigen CD69.

Jiménez-Fernández M, Rodríguez-Sinovas C, Cañes L, Ballester-Servera C, Vara A, Requena S, de la Fuente H, Martínez-González J, Sánchez-Madrid F. CD69-oxLDL ligand engagement induces Programmed Cell Death 1 (PD-1) expression in human CD4 + T lymphocytes. Cell Mol Life Sci. 2022 Aug 5;79(8):468. https://doi.org/10.1007/s00018-022-04481-1

BRITISH JOURNAL OF PHARMACOLOGY

CNIC SCIENTISTS IDENTIFY A NEUROPROTECTIVE ACTION OF METOPROLOL AFTER A STROKE

A drug costing just €2 a shot can protect the brain during a stroke and greatly reduce long-term incapacity. Metoprolol, a beta-blocker in routine use in cardiology for more than 40 years, has now been shown to have a specific neuroprotective effect.

Clemente-Moragón A, Oliver E, Calle D, Cussó L, Gómez M, Pradillo JM, Castejón R, Rallón N, Benito JM, Fernández-Ferro JC, Carneado-Ruíz J, Moro MA, Sánchez-González J, Fuster V, Cortés-Canteli M, Desco M, Ibáñez B. Neutrophil β1 adrenoceptor blockade blunts stroke-associated neuroinflammation. Br J Pharmacol. Epub 2022 Nov 20. Br J Pharmacol. 2023 Feb;180(4):459-478. https://doi.org/10.1111/bph.15963

JOURNAL OF CLINICAL INVESTIGATION

CNIC SCIENTISTS IDENTIFY A FACTOR THAT PROTECTS THE HEART AGAINST DAMAGE AFTER A HEART ATTACK

A study carried out at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) has identified a key factor that protects the heart after a heart attack. The study, led by Dr. Pilar Martín, who heads the Regulatory Molecules of Inflammatory Processes group at the CNIC, was published in the Journal of Clinical Investigation. The study shows that the expression of the receptor CD69 on regulatory T lymphocytes confers protection after a myocardial infarction by acting as a checkpoint for the exacerbated inflammation that causes medium-term cardiac injury.

Blanco-Domínguez R, de la Fuente H, Rodríguez C, Martín-Aguado L, Sánchez-Díaz R, Jiménez-Alejandre R, Rodríguez-Arabaolaza I, Curtabbi A, García-Guimaraes MM, Vera A, Rivero F, Cuesta J, Jiménez-Borreguero LJ, Cecconi A, Duran-Cambra A, Taurón M, Alonso J, Bueno H, Villalba-Orero M, Enríquez JA, Robson SC, Alfonso F, Sánchez-Madrid F, Martínez-González J, Martín P. CD69 expression on regulatory T cells protects from immune damage after myocardial infarction. J Clin Invest. 2022 Nov 1;132(21):e152418. https://doi.org/10.1172/JCI152418

NATURE CARDIOVASCULAR RESEARCH

CNIC SCIENTISTS IDENTIFY THE CAUSE OF ARRHYTHMIAS AND SUDDEN DEATH IN ANDERSEN-TAWIL SYNDROME TYPE 1

The Centro Nacional de Investigaciones Cardiovasculares (CNIC) has discovered the cause of arrhythmias and sudden death in the rare disease Andersen-Tawil syndrome type 1 (ATS1), which is caused by mutations affecting potassium channels that regulate electrical activity and the intracellular calcium cycle in cardiac and skeletal muscle.

Macías A, González-Guerra A, Moreno-Manuel AI, Cruz FM, Gutiérrez LK, García-Quintáns N, Roche-Molina M, Bermúdez-Jiménez F, Andrés V, Linarejos Vera-Pedrosa M, Martínez-Carrascoso I, Bernal JA, Jalife J. Kir2.1 dysfunction at the sarcolemma and the sarcoplasmic reticulum causes arrhythmias in a mouse model of Andersen–Tawil syndrome type 1. Nat Cardiovasc Res. 2022 Oct;1:900–917. https://doi.org/10.1038/s44161-022-00145-2

CIRCULATION

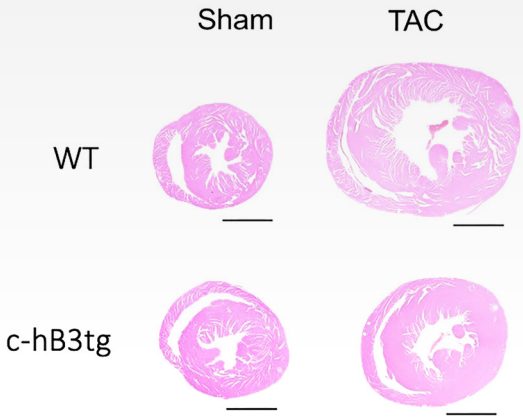
SPECIFIC MODIFIER GENES DETERMINE THE EFFECT OF MUTATIONS THAT CAUSE NON-COMPACTION CARDIOMYOPATHY

Non-compaction cardiomyopathy is a heart condition caused by defects that arise during fetal development and can have diverse health impacts in affected individuals, including sudden cardiac death. The Intercellular Signaling in Cardiovascular Development and Disease group at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) previously reported that this disease can be caused by two distinct mutations in the Mindbomb1 gene (Mib1).

Siguero-Álvarez M, Salguero-Jiménez A, Grego-Bessa J, de la Barrera J, MacGrogan D, Prados B, Sánchez-Sáez F, Piñeiro-Sabarís R, Felipe-Medina N, Torroja C, Gómez MJ, Sabater-Molina M, Escribá R, Richaud-Patin I, Iglesias-García O, Sbroggio M, Callejas S, O'Regan DP, McGurk KA, Dopazo A, Giovinazzo G, Ibañez B, Monserrat L, Pérez-Pomares JM, Sánchez-Cabo F, Pendas AM, Raya A, Gimeno-Blanes JR, de la Pompa JL. A Human Hereditary Cardiomyopathy Shares a Genetic Substrate with Bicuspid Aortic Valve. Circulation. Epub 2022 Nov 3. Circulation. 2023 Jan 3;147(1):47-65. https://doi.org/10.1161/CIRCULATIONAHA.121.058767

BASIC RESEARCH IN CARDIOLOGY

A NEW THERAPEUTIC TARGET FOR THE PREVENTION OF HEART FAILURE DUE TO AORTIC STENOSIS

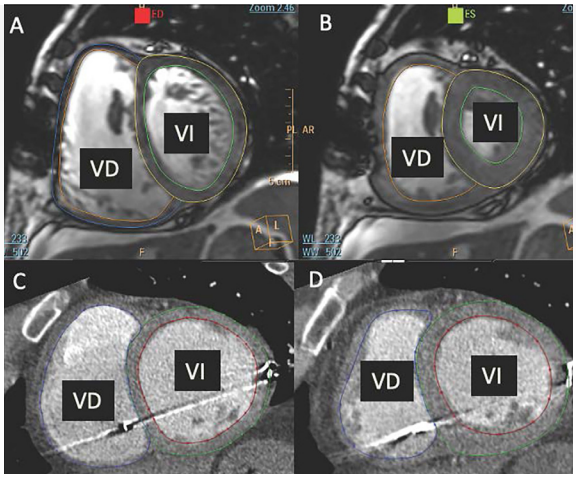


Scientists at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) have identified a new therapeutic target for the prevention of heart failure linked to aortic stenosis. The study was led by Dr. Borja Ibáñez, Clinical Research Director at the CNIC, cardiologist at Hospital Universitario Fundación Jiménez Díaz, and member of the Spanish cardiovascular research network (CIBERCV). The study shows that overexpression in cardiac muscle cells of beta-3 adrenergic receptor, a member of the beta adrenergic system, can prevent or even reverse heart failure in a mouse model of aortic stenosis, a condition that currently has few therapeutic options.

Pun-García A, Clemente-Moragón A, Villena-Gutierrez R, Gómez M, Sanz-Rosa D, Díaz-Guerra A, Prados B, Medina JP, Montó F, Ivorra MD, Márquez-López C, Cannavo A, Bernal JA, Koch WJ, Fuster V, de la Pompa JL, Oliver E, Ibanez B. Beta-3 adrenergic receptor overexpression reverses aortic stenosis-induced heart failure and restores balanced mitochondrial dynamics. Basic Res Cardiol. 2022 Nov 29;117(1):62. https://doi.org/10.1007/s00395-022-00966-z

EUROPEAN JOURNAL OF HEART FAILURE

A PROMISING DRUG TREATMENT FOR PATIENTS WITH PULMONARY HYPERTENSION ASSOCIATED WITH HEART DISEASE



There is currently no specific treatment for pulmonary hypertension associated with heart disease, a highly prevalent condition with a poor prognosis. Now, a study from the Centro Nacional de Investigaciones Cardiovasculares (CNIC) and Hospital Clínic de Barcelona/IDIBAPS has shown that mirabegron, a drug that acts on the beta-3 adrenergic receptor, may have a beneficial effect on right ventricular function.

García-Álvarez A, Blanco I, García-Lunar I, Jordà P, Rodriguez-Arias JJ, Fernández-Friera L, Zegri I, Nuche J, Gomez-Bueno M, Prat S, Pujadas S, Sole-Gonzalez E, Garcia-Cossio MD, Rivas M, Torrecilla E, Pereda D, Sanchez J, García-Pavía P, Segovia-Cubero J, Delgado JF, Mirabet S, Fuster V, Barberá JA, Ibañez B; SPHERE-HF Investigators. β3 adrenergic agonist treatment in chronic pulmonary hypertension associated with heart failure (SPHERE-HF): a double blind, placebo-controlled, randomized clinical trial. Eur J Heart Fail. Epub 2022 Dec 4. Eur J Heart Fail. 2023 Mar;25(3):373-385. https://doi.org/10.1002/ejhf.2745

ELIFE

CNIC SCIENTISTS IDENTIFY THE ESSENTIAL ROLE OF CELL-SURFACE "NANOFOLDS" AND "GLUE" IN THE MECHANICAL RESPONSE OF CELLS

A study at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) has revealed that subcellular structures called caveolae play an essential role in cell mechanics. The results suggest that impaired caveolar function could be involved in a variety of processes, including platelet aggregation, cardiovascular disease, fibrosis, and tumor formation

Lolo FN, Pavón DM, Grande A, Elósegui Artola A, Segatori VI, Sánchez S, Trepat X, Roca-Cusachs P, Del Pozo MA. Caveolae couple mechanical stress to integrin recycling and activation. Elife. 2022 Oct 20;11:e82348. https://doi.org/10.7554/eLife.82348

BLOOD

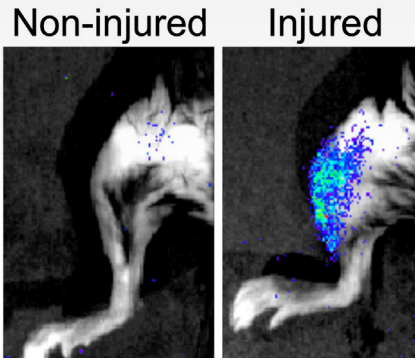
RXR, THE CELL PROTEIN THAT KEEPS BLOOD STEM CELLS YOUNG AND FIT

The cell protein retinoid X receptor (RXR) is a key factor in the maintenance of hematopoietic stem cells, the immature stem cells that give rise to all the blood cell lineages. RXR ensures that these cells remain youthful and fit, thereby reducing the risk of developing myeloproliferative syndromes as the body ages.

Menéndez-Gutiérrez MP, Porcuna J, Nayak R, Paredes A, Niu H, Núñez V, Paranjpe A, Gómez MJ, Bhattacharjee A, Schnell DJ, Sánchez-Cabo F, Welch JS, Salomonis N, Cancelas JA, Ricote M. Retinoid X receptor promotes hematopoietic stem cell fitness and quiescence and preserves hematopoietic homeostasis. Blood. Epub Nov 2022. Blood. 2023 Feb 9;141(6):592-608. https://doi.org/10.1182/blood.2022016832

NATURE

RESEARCHERS CHARACTERIZE RARE, DAMAGED CELLS THAT BLOCK THE FUNCTIONS OF THEIR NEIGHBOUR HEALTHY CELLS AND IDENTIFY WAYS TO NEUTRALIZE THEM AND IMPROVE TISSUE REGENERATION

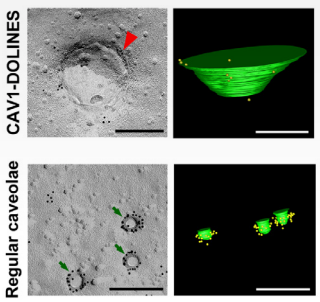


Researchers at the Universitat Pompeu Fabra (UPF), ICREA, CIBERNED, CNIC and Altos Labs, among other national and international collaborators, have characterized how damaged cells (senescent cells) that inevitably arise after injury negatively impact tissue regeneration, and how this mechanism operates actively in old age, but surprisingly also in young age. This negative action can be overcome genetically and pharmacologically, hence restoring stem cell regenerative functions.

Moiseeva V, Cisneros A, Sica V, Deryagin O, Lai Y, Jung S, Andrés E, An J, Segalés J, Ortet L, Lukesova V, Volpe G, Benguria A, Dopazo A, Benitah SA, Urano Y, Del Sol A, Esteban MA, Ohkawa Y, Serrano AL, Perdiguero E, Muñoz-Cánoves P. Senescence atlas reveals an aged-like inflamed niche that blunts muscle regeneration. Nature. Epub 2022 Dec 21. Nature. 2023 Jan;613(7942):169-178. https://doi.org/10.1038/s41586-022-05535-x

NATURE CELL BIOLOGY

A CNIC STUDY SHOWS THAT CELLS POSSESS 2 MECHANISMS TO ALLOW THEM TO RESPOND TO DIFFERENT FORCE RANGES



A study carried out at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) heralds a paradigm change in the field of mechanobiology. The study reveals that cells respond to forces of differing strength using use two distinct mechanisms, one mediated by minute, cup-like invaginations on the cell surface called caveolae and the other by newly discovered large membrane depressions the study authors call dolines.

Lolo FN, Walani N, Seemann E, Zalvidea D, Pavón DM, Cojoc G, Zamai M, Viaris de Lesegno C, Martínez de Benito F, Sánchez-Álvarez M, Uriarte JJ, Echarri A, Jiménez-Carretero D, Escolano JC, Sánchez SA, Caiolfa VR, Navajas D, Trepat X, Guck J, Lamaze C, Roca-Cusachs P, Kessels MM, Qualmann B, Arroyo M, Del Pozo MA. Caveolin-1 dolines form a distinct and rapid caveolae-independent mechanoadaptation system. Nat Cell Biol. Epub 2022 Dec 21. Nat Cell Biol. 2023 Jan;25(1):120-133. https://doi.org/10.1038/s41556-022-01034-3